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- (71) Applicant (for all designated States except US): GENESIS RESEARCH & DEVELOPMENT CORPORATION LIMITED [NZ/NZ]; 1 Fox Street, Parnell, Auckland (NZ).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): WATSON, James, D. [NZ/NZ]; 769 Riddell Road, St Heliers, Auckland (NZ). STRACHAN, Lorna [GB/NZ]; 4B/94 Nelson Street, Auckland City (NZ). SLEEMAN, Matthew [GB/GB]; c/-Cambridge Antibody Technology, Cambridge House, The Science Park, Melbourn Royston, Cambridgeshire, SG8 6JJ (GB). ONRUST, Rene [NZ/NZ]; 21 Duart Avenue, Mt Albert, Auckland (NZ). MURISON, James, Greg [NZ/NZ]; 24 Calgary Street, Sandringham, Auckland (NZ). KUMBLE, Krishanand, D. [IN/US]; 2301 S Millbend Drive #706, The Woodlands, TX 77380 (US).

- (74) Agents: HAWKINS, Michael, Howard et al.; Baldwin Shelston Waters, P.O. Box 852, Wellington (NZ).
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(54) Title: COMPOSITIONS ISOLATED FROM SKIN CELLS AND METHODS FOR THEIR USE

(57) Abstract: Isolated polynucleotides encoding polypeptides expressed in mammalian skin cells are provided, together with expression vectors and host cells comprising such isolated polynucleotides. Methods for the use of such polynucleotides and polypeptides are also provided.

COMPOSITIONS ISOLATED FROM SKIN CELLS AND METHODS FOR THEIR USE

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Technical Field of the Invention

This invention relates to polynucleotides, polypeptides, polypeptides expressed in skin cells, and various methods for treating a patient involving administration of a polypeptide or polynucleotide of the present invention.

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Background of the Invention

The skin is the largest organ in the body and serves as a protective cover. The loss of skin, as occurs in a badly burned person, may lead to death owing to the absence of a barrier against infection by external microbial organisms, as well as loss of body temperature and body fluids.

Skin tissue is composed of several layers. The outermost layer is the epidermis which is supported by a basement membrane and overlies the dermis. Beneath the dermis is loose connective tissue and fascia which cover muscles or bony tissue. The skin is a self-renewing tissue in that cells are constantly being formed and shed. The deepest cells of the epidermis are the basal cells, which are enriched in cells capable of replication. Such replicating cells are called progenitor or stem cells. Replicating cells in turn give rise to daughter cells called 'transit amplifying cells'. These cells undergo differentiation and maturation into keratinocytes (mature skin cells) as they move from the basal layer to the more superficial layers of the epidermis. In the process, keratinocytes become cornified and are ultimately shed from the skin surface. Other cells in the epidermis include melanocytes which synthesize melanin, the pigment responsible for protection against sunlight. The Langerhans cell also resides in the epidermis and functions as a cell which processes foreign proteins for presentation to the immune system.

The dermis contains nerves, blood and lymphatic vessels, fibrous and fatty tissue. Within the dermis are fibroblasts, macrophages and mast cells. Both the epidermis and dermis are penetrated by sweat, or sebaceous glands and hair follicles. Each strand of hair is derived from a hair follicle. When hair is plucked out, the hair re-grows from epithelial cells directed by the dermal papillae of the hair follicle.

When the skin surface is breached, for example in a wound, the stem cells proliferate and daughter keratinocytes migrate across the wound to reseal the tissues. The skin cells therefore possess genes activated in response to trauma. The products of these genes include several growth factors, such as epidermal growth factor, which mediate the proliferation of skin cells. The genes that are activated in the skin, and the protein products of such genes, may be developed as agents for the treatment of skin wounds. Additional growth factors derived from skin cells may also influence growth of other cell types. As skin cancers are a disorder of the growth of skin cells, proteins derived from skin that regulate cellular growth may be developed as agents for the treatment of skin cancers. Skin derived proteins that regulate the production of melanin may be useful as agents, which protect skin against unwanted effects of sunlight.

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Keratinocytes are known to secrete cytokines and express various cell surface proteins. Cytokines and cell surface molecules are proteins, which play an important role in the inflammatory response against infection, and also in autoimmune diseases affecting the skin. Genes and their protein products that are expressed by skin cells may thus be developed into agents for the treatment of inflammatory disorders affecting the skin.

Hair is an important part of a person's individuality. Disorders of the skin may lead to hair loss. Alopecia areata is a disease characterized by the patchy loss of hair over the scalp. Total baldness is a side effect of drug treatment for cancer. The growth and development of hair is mediated by the effects of genes expressed in skin and dermal papillae. Such genes and their protein products may be usefully developed into agents for the treatment of disorders of the hair follicle.

New treatments are required to hasten the healing of skin wounds, to prevent the loss of hair, enhance the re-growth of hair or removal of hair, and to treat autoimmune

and inflammatory skin diseases more effectively and without adverse effects. More effective treatments of skin cancers are also required. There thus remains a need in the art for the identification and isolation of genes encoding proteins expressed in the skin, for use in the development of therapeutic agents for the treatment of disorders including those associated with skin.

Summary of the Invention

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The present invention provides polypeptides and functional portions of polypeptides, which may be expressed in skin cells, together with polynucleotides encoding such polypeptides or functional portions thereof, expression vectors and host cells comprising such polynucleotides, and methods for their use.

In specific embodiments, isolated polynucleotides are provided that comprise a polynucleotide selected from the group consisting of: (a) sequences recited in SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; (b) complements of the sequences recited in SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; (c) reverse complements of the sequences recited in SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; (d) reverse sequences of the sequences recited in SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; (e) sequences having a 99% probability of being the same as a sequence of (a)-(d); and (f) sequences having at least 50%, 75%, 90% or 95% identity to a sequence of (a)-(d).

In further embodiments, the present invention provides isolated polypeptides comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725, together with isolated polypucleotides encoding such polypeptides. Isolated polypeptides which

comprise at least a functional portion of a polypeptide comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725; and (b) sequences having 50%, 75% or 90% identity to a sequence of SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725, are also provided.

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In related embodiments, the present invention provides expression vectors comprising the above polynucleotides, together with host cells transformed with such vectors.

In a further aspect, the present invention provides a method of stimulating keratinocyte growth and motility, inhibiting the growth of epithelial-derived cancer cells, inhibiting angiogenesis and vascularization of tumors, or modulating the growth of blood vessels in a subject, comprising administering to the subject a composition comprising an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398.

Methods for modulating skin inflammation in a subject are also provided, the methods comprising administering to the subject a composition comprising an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 338 and 347; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 338 and 347. In an additional aspect, the present invention provides methods for stimulating the growth of epithelial cells in a subject. Such methods comprise administering to the subject a composition comprising an isolated polypeptide including an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 129 and 348; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 129 and 348.

In yet a further aspect, methods for inhibiting the binding of HIV-1 to leukocytes, for the treatment of an inflammatory disease or for the treatment of cancer in a subject are provided, the methods comprising administering to the subject a composition comprising an isolated polypeptide including an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 340, 344, 345 and 346; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEO ID NOS: 340, 344, 345 and 346.

As detailed below, the isolated polynucleotides and polypeptides of the present invention may be usefully employed in the preparation of therapeutic agents for the treatment of skin disorders.

The above-mentioned and additional features of the present invention, together with the manner of obtaining them, will be best understood by reference to the following more detailed description. All references disclosed herein are incorporated herein by reference in their entirety as if each was incorporated individually.

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Brief Description of the Drawings

Fig. 1 shows the results of a Northern analysis of the distribution of huTR1 mRNA in human tissues. Key: He, Heart; Br, Brain; Pl, Placenta; Lu, Lung; Li, Liver; SM, Skeletal muscle; Ki, Kidney; Sp, Spleen; Th, Thymus; Pr, Prostate; Ov, Ovary.

MuTR1a (500ng/ml), huTR1a (100ng/ml) or LPS (3pg/ml) were added as described in the text.

Fig. 2 shows the results of a MAP kinase assay of muTR1a and huTR1a.

- Fig. 3 shows the stimulation of growth of neonatal foreskin keratinocytes by muTR1a.
- Fig. 4 shows the stimulation of growth of the transformed human keratinocyte cell line HaCaT by muTR1a and huTR1a.
- Fig. 5 shows the inhibition of growth of the human epidermal carcinoma cell line A431 by muTR1a and huTR1a.
 - Fig. 6 shows the inhibition of IL-2 induced growth of concanavalin A-stimulated

murine splenocytes by KS2a.

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Fig. 7 shows the stimulation of growth of rat intestinal epithelial cells (IEC-18) by a combination of KS3a plus apo-transferrin.

Fig. 8 illustrates the oxidative burst effect of TR-1 (100 ng/ml), muKS1 (100 ng/ml), SDF1α (100 ng/ml), and fMLP (10 μM) on human PBMC.

Figure 9 shows the chemotactic effect of muKS1 and SDF-1α on THP-1 cells.

Figure 10 shows the induction of cellular infiltrate in C3H/HeJ mice after intraperitoneal injections with muKS1 (50 μ g), GV14B (50 μ g) and PBS.

Figure 11 demonstrates the induction of phosphorylation of ERK1 and ERK2 in CV1/EBNA and HeLa cell lines by huTR1a.

Figure 12 shows the huTR1 mRNA expression in HeLa cells after stimulation by muTR1, huTGFα and PBS (100 ng/ml each).

Figure 13 shows activation of the SRE by muTR1a in PC-12 (Fig. 13A) and HaCaT (Fig. 13B) cells.

Figure 14 shows the inhibition of huTR1a mediated growth on HaCaT cells by an antibody to the EGF receptor.

Figure 15A shows the nucleotide sequence of KS1 cDNA (SEQ ID NO: 464) along with the deduced amino acid sequence (SEQ ID NO: 465) using single letter code. The 5' UTR is indicated by negative numbers. The underlined NH₂-terminal amino acids represent the predicted leader sequence and the stop codon is denoted by ***. The polyadenylation signal is marked by a double underline. Figure 15B shows a comparison of the complete open reading frame of KS1 (referred to in Fig. 15B as KLF-1) with its human homologue BRAK and with the mouse α-chemokines mCrg-2, mMig, mSDF-1, mBLC, mMIP2, mKC and mLIX. An additional five residues are present in KS1 and BRAK between cysteine 3 and cysteine 4 that have not previously been described for chemokines.

Detailed Description of the Invention

In one aspect, the present invention provides polynucleotides that were isolated from mammalian skin cells. As used herein, the term "polynucleotide" means a single or

double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and RNA molecules, both sense and anti-sense strands. The term comprehends cDNA, genomic DNA, recombinant DNA and wholly or partially synthesized nucleic acid molecules. A polynucleotide may consist of an entire gene, or a portion thereof. A gene is a DNA sequence that codes for a functional protein or RNA molecule. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all operable anti-sense fragments. Anti-sense polynucleotides and techniques involving anti-sense polynucleotides are well known in the art and are described, for example, in Robinson-Benion et al., "Anti-sense Techniques," *Methods in Enzymol.* 254(23):363-375, 1995; and Kawasaki et al., *Artific. Organs* 20(8):836-848, 1996.

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Identification of genomic DNA and heterologous species DNAs can be accomplished by standard DNA/DNA hybridization techniques, under appropriately stringent conditions, using all or part of a cDNA sequence as a probe to screen an appropriate library. Alternatively, PCR techniques using oligonucleotide primers that are designed based on known genomic DNA, cDNA and protein sequences can be used to amplify and identify genomic and cDNA sequences. Synthetic DNAs corresponding to the identified sequences and variants may be produced by conventional synthesis methods. All the polynucleotides provided by the present invention are isolated and purified, as those terms are commonly used in the art.

In specific embodiments, the polynucleotides of the present invention comprise a sequence selected from the group consisting of sequences provided in SEQ ID NOS: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623, and variants of the sequences of SEQ ID NOS: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623. Polynucleotides that comprise complements of such sequences, reverse complements of such sequences, or reverse sequences of such sequences, together with variants of such sequences, are also provided.

The definition of the terms "complement," "reverse complement," and "reverse sequence," as used herein, is best illustrated by the following example. For the sequence 5' AGGACC 3', the complement, reverse complement, and reverse sequence are as follows:

complement 3' 7

3' TCCTGG 5'

reverse complement

3' GGTCCT 5'

reverse sequence

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5' CCAGGA 3'.

As used herein, the term "complement" refers to sequences that are fully complementary to a sequence disclosed herein.

In another aspect, the present invention provides isolated polypeptides and functional portions of polypeptides encoded, or partially encoded, by the above polynucleotides. As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins, wherein the amino acid residues are linked by covalent peptide bonds. The term "polypeptide encoded by a polynucleotide" as used herein, includes polypeptides encoded by a polynucleotide which comprises a partial isolated DNA sequence provided herein. In specific embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725, as well as variants of such sequences.

Polypeptides of the present invention may be produced recombinantly by inserting a DNA sequence that encodes the polypeptide into an expression vector and expressing the polypeptide in an appropriate host. Any of a variety of expression vectors known to those of ordinary skill in the art may be employed. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, insect, yeast, or a mammalian cell line such as COS or CHO. The DNA sequences expressed in this manner may encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof.

In a related aspect, polypeptides are provided that comprise at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512-513 and 624-725, and variants thereof. As used herein, the "functional portion" of a polypeptide is that portion which contains the active site essential for affecting the function of the polypeptide, for example, the portion of the molecule that is capable of binding one or more reactants. The active site may be made up of separate portions present on one or more polypeptide chains and will generally exhibit high binding affinity.

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Functional portions of a polypeptide may be identified by first preparing fragments of the polypeptide by either chemical or enzymatic digestion of the polypeptide, or by mutation analysis of the polynucleotide that encodes the polypeptide and subsequent expression of the resulting mutant polypeptides. The polypeptide fragments or mutant polypeptides are then tested to determine which portions retain biological activity, using, for example, the representative assays provided below.

Portions and other variants of the inventive polypeptides may also be generated by synthetic or recombinant means. Synthetic polypeptides having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems, Inc. (Foster City, California), and may be operated according to the manufacturer's instructions. Variants of a native polypeptide may be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (Kunkel, T., Proc. Natl. Acad. Sci. USA 82:488-492, 1985). Sections of DNA sequence

may also be removed using standard techniques to permit preparation of truncated polypeptides.

In general, the polypeptides disclosed herein are prepared in an isolated, substantially pure, form. Preferably, the polypeptides are at least about 80% pure, more preferably at least about 90% pure, and most preferably at least about 99% pure. In certain preferred embodiments, described in detail below, the isolated polypeptides are incorporated into pharmaceutical compositions or vaccines for use in the treatment of skin disorders.

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As used herein, the term "variant" comprehends nucleotide or amino acid sequences different from the specifically identified sequences, wherein one or more nucleotides or amino acid residues is deleted, substituted, or added. Variants may be naturally occurring allelic variants, or non-naturally occurring variants. In certain preferred embodiments, variants of the inventive sequences retain certain, or all, of the functional characteristics of the inventive sequence. Variant sequences (polynucleotide or polypeptide) preferably exhibit at least 50%, more preferably at least 75%, and most preferably at least 90% or 95% identity to a sequence of the present invention. The percentage identity is determined by aligning the two sequences to be compared as described below, determining the number of identical residues in the aligned portion, dividing that number by the total number of residues in the inventive (queried) sequence, and multiplying the result by 100.

Polynucleotide or polypeptide sequences may be aligned, and percentages of identical nucleotides in a specified region may be determined against another polynucleotide or polypeptide, using computer algorithms that are publicly available. Two exemplary algorithms for aligning and identifying the similarity of polynucleotide sequences are the BLASTN and FASTA algorithms. The alignment and similarity of polypeptide sequences may be examined using the BLASTP and algorithm. BLASTX and FASTX algorithms compare nucleotide query sequences translated in all reading frames against polypeptide sequences. The BLASTN, BLASTP and BLASTX algorithms are available on the NCBI anonymous FTP server (ftp://ncbi.nlm.nih.gov)

under /blast/executables/ and are available from the National Center for Biotechnology Information (NCBI), National Library of Medicine, Building 38A, Room 8N805, Bethesda, MD 20894 USA.

The FASTA and FASTX algorithms are available on the Internet at the ftp site ftp://ftp.Virginia.edu/pub/. The FASTA software package is also available from the University of Virginia by contacting David Hudson, Assistant Provost for Research, University of Virginia, PO Box 9025, Charlottesville, VA 22906-9025. The FASTA algorithm, set to the default parameters described in the documentation and distributed with the algorithm, may be used in the determination of polynucleotide variants. The readme files for FASTA and FASTX v1.0x that are distributed with the algorithms describe the use of the algorithms and describe the default parameters. The use of the FASTA and FASTX algorithms is also described in Pearson, and Lipman, *Proc. Natl. Acad. Sci. USA* 85:2444-2448, 1988; and Pearson, *Methods in Enzymol.* 183:63-98, 1990.

The BLASTN algorithm version 2.0.4 [Feb-24-1998], 2.0.6 [Sept-16-1998] and 2.0.11 [Jan-20-2000], set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of polynucleotide variants according to the present invention. The BLASTP algorithm version 2.0.4, 2.0.6 and 2.0.11, set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of polypeptide variants according to the present invention. The use of the BLAST family of algorithms, including BLASTN, BLASTP and BLASTX is described in the publication of Altschul, et al., Nucleic Acids Res. 25:3389-3402, 1997.

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The following running parameters are preferred for determination of alignments and similarities using BLASTN that contribute to the E values and percentage identity for polynucleotides: Unix running command with default parameters thus: blastall -p blastn - d embldb -e 10 -G 0 -E 0 -r 1 -v 30 -b 30 -i queryseq -o results; and parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero

invokes default behavior) [Integer]; -r Reward for a nucleotide match (blastn only) [Integer]; -v Number of one-line descriptions (V) [Integer]; -b Number of alignments to show (B) [Integer]; -i Query File [File In]; -o BLAST report Output File [File Out] Optional. The following running parameters are preferred for determination of alignments and similarities using BLASTP that contribute to the E values and percentage identity for polypeptides: blastall -p blastp -d swissprotdb -e 10 -G 1 -E 11 -r 1 -v 30 -b 30 -i queryseq -o results; and the parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero invokes default behavior) [Integer]; -v Number of one-line descriptions (v) [Integer]; -b Number of alignments to show (b) [Integer]; -I Query File [File In]; -o BLAST report Output File [File Out] Optional.

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The "hits" to one or more database sequences by a queried sequence produced by BLASTN, BLASTP, FASTA, or a similar algorithm, align and identify similar portions of sequences. The hits are arranged in order of the degree of similarity and the length of sequence overlap. Hits to a database sequence generally represent an overlap over only a fraction of the sequence length of the queried sequence.

As noted above, the percentage identity of a polynucleotide or polypeptide sequence is determined by aligning polynucleotide and polypeptide sequences using appropriate algorithms, such as BLASTN or BLASTP, respectively, set to default parameters; identifying the number of identical nucleic or amino acids over the aligned portions; dividing the number of identical nucleic or amino acids by the total number of nucleic or amino acids of the polynucleotide or polypeptide of the present invention; and then multiplying by 100 to determine the percentage identity. By way of example, a queried polynucleotide having 220 nucleic acids has a hit to a polynucleotide sequence in the EMBL database having 520 nucleic acids over a stretch of 23 nucleotides in the alignment produced by the BLASTN algorithm using the default parameters. The 23 nucleotide hit includes 21 identical nucleotides, one gap and one different nucleotide. The percentage identity of the queried polynucleotide to the hit in the EMBL database is

thus 21/220 times 100, or 9.5%. The identity of polypeptide sequences may be determined in a similar fashion.

The BLASTN and BLASTX algorithms also produce "Expect" values for polynucleotide and polypeptide alignments. The Expect value (E) indicates the number of hits one can "expect" to see over a certain number of contiguous sequences by chance when searching a database of a certain size. The Expect value is used as a significance threshold for determining whether the hit to a database indicates true similarity. For example, an E value of 0.1 assigned to a polynucleotide hit is interpreted as meaning that in a database of the size of the EMBL database, one might expect to see 0.1 matches over the aligned portion of the sequence with a similar score simply by chance. By this criterion, the aligned and matched portions of the sequences then have a probability of 90% of being the same. For sequences having an E value of 0.01 or less over aligned and matched portions, the probability of finding a match by chance in the EMBL database is 1% or less using the BLASTN algorithm. E values for polypeptide sequences may be determined in a similar fashion using various polypeptide databases, such as the SwissProt database.

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According to one embodiment, "variant" polynucleotides and polypeptides, with reference to each of the polynucleotides and polypeptides of the present invention, preferably comprise sequences having the same number or fewer nucleic or amino acids than each of the polynucleotides or polypeptides of the present invention and producing an E value of 0.01 or less when compared to the polynucleotide or polypeptide of the present invention. That is, a variant polynucleotide or polypeptide is any sequence that has at least a 99% probability of being the same as the polynucleotide or polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTN or BLASTX algorithms set at the default parameters. According to a preferred embodiment, a variant polynucleotide is a sequence having the same number or fewer nucleic acids than a polynucleotide of the present invention that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using the BLASTN algorithm set at the default

parameters. Similarly, according to a preferred embodiment, a variant polypeptide is a sequence having the same number or fewer amino acids than a polypeptide of the present invention that has at least a 99% probability of being the same as the polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTP algorithm set at the default parameters.

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Variant polynucleotide sequences will generally hybridize to the recited polynucleotide sequences under stringent conditions. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65 °C and two washes of 30 minutes each in 0.2X SSC, 0.1% SDS at 65 °C.

As used herein, the term "x-mer," with reference to a specific value of "x," refers to a polynucleotide or polypeptide, respectively, comprising at least a specified number ("x") of contiguous residues of: any of the polynucleotides provided in SEQ ID NO: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; or any of the polypeptides set out in SEQ ID NO: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725. The value of x may be from about 20 to about 600, depending upon the specific sequence.

Polynucleotides of the present invention comprehend polynucleotides comprising at least a specified number of contiguous residues (x-mers) of any of the polynucleotides identified as SEQ ID NO: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623, or their variants. Polypeptides of the present invention comprehend polypeptides comprising at least a specified number of contiguous residues (x-mers) of any of the polypeptides identified as SEQ ID NO: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725. According to preferred embodiments, the value of x is at least 20, more preferably at least 40, more preferably yet at least 60, and most preferably at least 80. Thus, polynucleotides of the present invention include polynucleotides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a

250-mer; or a 300-mer, 400-mer, 500-mer or 600-mer of a polynucleotide provided in SEQ ID NOS: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623, or of a variant of one of the polynucleotides provided in SEQ ID NO: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623. Polypeptides of the present invention include polypeptides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer; or a 300-mer, 400-mer, 500-mer or 600-mer of a polypeptide provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725, or of a variant of one of the polypeptides provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725.

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The inventive polynucleotides may be isolated by high throughput sequencing of cDNA libraries prepared from mammalian skin cells as described below in Example 1. Alternatively, oligonucleotide probes based on the sequences provided in SEQ ID NOS: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623 can be synthesized and used to identify positive clones in either cDNA or genomic DNA libraries from mammalian skin cells by means of hybridization or polymerase chain reaction (PCR) techniques. Probes can be shorter than the sequences provided herein but should be at least about 10, preferably at least about 15 and most preferably at least about 20 nucleotides in length. Hybridization and PCR techniques suitable for use with such oligonucleotide probes are well known in the art (see, for example, Mullis, et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlieh, ed., PCR Technology, Stockton Press: NY, 1989; (Sambrook, J, Fritsch, EF and Maniatis, T, eds., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor: New York, 1989). Positive clones may be analyzed by restriction enzyme digestion, DNA sequencing or the like.

In addition, DNA sequences of the present invention may be generated by synthetic means using techniques well known in the art. Equipment for automated synthesis of oligonucleotides is commercially available from suppliers such as Perkin

Elmer/Applied Biosystems Division (Foster City, California) and may be operated according to the manufacturer's instructions.

Since the polynucleotide sequences of the present invention have been derived from skin, they likely encode proteins that have important roles in growth and development of skin, and in responses of skin to tissue injury and inflammation as well as disease states. Some of the polynucleotides contain sequences that code for signal sequences, or transmembrane domains, which identify the protein products as secreted molecules or receptors. Such protein products are likely to be growth factors, cytokines, or their cognate receptors. Several of the polypeptide sequences have more than 25% similarity to known biologically important proteins and thus are likely to represent proteins having similar biological functions.

In particular, the inventive polypeptides have important roles in processes such as: induction of hair growth; differentiation of skin stem cells into specialized cell types; cell migration; cell proliferation and cell-cell interaction. The polypeptides are important in the maintenance of tissue integrity, and thus are important in processes such as wound healing. Some of the disclosed polypeptides act as modulators of immune responses, especially since immune cells are known to infiltrate skin during tissue insult causing growth and differentiation of skin cells. In addition, many polypeptides are immunologically active, making them important therapeutic targets in a whole range of disease states not only within skin, but also in other tissues of the body. Antibodies to the polypeptides of the present invention and small molecule inhibitors related to the polypeptides of the present invention may also be used for modulating immune responses and for treatment of diseases according to the present invention.

In one aspect, the present invention provides methods for using one or more of the inventive polypeptides or polynucleotides to treat disorders in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human.

In this aspect, the polypeptide or polynucleotide is generally present within a pharmaceutical or immunogenic composition. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above

sequences (or variants thereof), and a physiologically acceptable carrier. Immunogenic compositions may comprise one or more of the above polypeptides and a non-specific immune response amplifier, such as an adjuvant or a liposome, into which the polypeptide is incorporated.

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Alternatively, a pharmaceutical or immunogenic composition of the present invention may contain DNA encoding one or more polypeptides as described above, such that the polypeptide is generated in situ. In such compositions, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, and bacterial and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminator signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerin) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other poxvirus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic, or defective, replication competent virus. Techniques for incorporating DNA into such expression systems are well known in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

Routes and frequency of administration, as well as dosage, vary from individual to individual. In general, the pharmaceutical and immunogenic compositions may be administered by injection (e.g., intradermal, intramuscular, intravenous, or subcutaneous), intranasally (e.g., by aspiration) or orally. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg per kg of host, and preferably from about 100 pg to about 1 µg per kg of host. Suitable dose

sizes will vary with the size of the patient, but will typically range from about 0.1 ml to about 5 ml.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax, or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactic galactide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

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Any of a variety of adjuvants may be employed in the immunogenic compositions of the invention to non-specifically enhance the immune response. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a non-specific stimulator of immune responses, such as lipid A, Bordetella pertussis, or Mycobacterium tuberculosis. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Freund's Complete Adjuvant (Difco Laboratories, Detroit, Michigan), and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, New Jersey). Other suitable adjuvants include alum, biodegradable microspheres, monophosphoryl lipid A, and Quil A.

The polynucleotides of the present invention may also be used as markers for tissue, as chromosome markers or tags, in the identification of genetic disorders, and for the design of oligonucleotides for examination of expression patterns using techniques well known in the art, such as the microarray technology available from Affymetrix (Santa Clara, CA). Partial polynucleotide sequences disclosed herein may be employed to obtain full length genes by, for example, screening of DNA expression libraries using hybridization probes or PCR primers based on the inventive sequences.

The polypeptides provided by the present invention may additionally be used in assays to determine biological activity, to raise antibodies, to isolate corresponding ligands or receptors, in assays to quantitatively determine levels of protein or cognate corresponding ligand or receptor, as anti-inflammatory agents, and in compositions for skin, connective tissue and/or nerve tissue growth or regeneration. The present invention further provides methods for modulating expression of the inventive polypeptides, for example by inhibiting translation of the relevant polynucleotide. Translation of the relevant polynucleotide may be inhibited, for example, by introducing anti-sense expression vectors; by introducing antisense oligodeoxyribonucleotides or antisense phosphorothioate oligodeoxyribonucleotides; by introducing antisense oligoribonucleotides or antisense phosphorothioate oligoribonucleotides; or by other means which are well known in the art. Cell permeation and activity of antisense oligonucleotides can be enhanced by appropriate chemical modifications, such as the use of phenoxazine-substituted C-5 propynyl uracil oligonucleotides (Flanagan et al., (1999) Nat. Biotechnol. 17 (1): 48-52) or 2'-O-(2-methoxy) ethyl (2'-MOE)-oligonucleotides (Zhang et al., (2000) Nat. Biotechnol. 18: 862-867). The use of techniques involving antisense polynucleotides is well known in the art and is described, for example, in Robinson-Benion et al. (1995), Antisense techniques, Methods in Enzymol. 254 (23): 363-375 and Kawasaki et al. (1996), Artific. Organs 20 (8): 836-848.

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The following Examples are offered by way of illustration and not by way of limitation.

Example 1

ISOLATION OF CDNA SEQUENCES FROM SKIN CELL EXPRESSION LIBRARIES

The cDNA sequences of the present invention were obtained by high-throughput sequencing of cDNA expression libraries constructed from specialized rodent or human skin cells as shown in Table 1.

Table 1

Library	Skin cell type	Source
DEPA	dermal papilla	rat

SKTC	keratinocytes	human
HNFF	neonatal foreskin fibroblast	human
MEMS	embryonic skin	mouse
KSČL	keratinocyte stem cell	mouse
TRAM	transit amplifying cells	mouse
MFSE	epidermis	mouse
·HLEA	small epithelial airway cells	human
HLEB	small epithelial airway cells	human
HNKA	NK cells	human

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These cDNA libraries were prepared as described below.

cDNA Library from Dermal Papilla (DEPA)

Dermal papilla cells from rat hair vibrissae (whiskers) were grown in culture and the total RNA extracted from these cells using established protocols. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, California), according to the manufacturer's specifications. A cDNA expression library was then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA Library from Keratinocytes (SKTC)

Keratinocytes obtained from human neonatal foreskins (Mitra, R and Nikoloff, B in *Handbook of Keratinocyte Methods*, pp. 17-24, 1994) were grown in serum-free KSFM (BRL Life Technologies) and harvested along with differentiated cells (10⁸ cells). Keratinocytes were allowed to differentiate by addition of fetal calf serum at a final concentration of 10% to the culture medium and cells were harvested after 48 hours. Total RNA was isolated from the two cell populations using TRIzol Reagent (BRL Life Technologies) and used to obtain mRNA using a Poly(A) Quik mRNA isolation kit

(Stratagene). cDNAs expressed in differentiated keratinocytes were enriched by using a PCR-Select cDNA Subtraction Kit (Clontech, Palo Alto, California). Briefly, mRNA was obtained from either undifferentiated keratinocytes ("driver mRNA") or differentiated keratinocytes ("tester mRNA") and used to synthesize cDNA. The two populations of cDNA were separately digested with *RsaI* to obtain shorter, blunt-ended molecules. Two tester populations were created by ligating different adaptors at the cDNA ends and two successive rounds of hybridization were performed with an excess of driver cDNA. The adaptors allowed for PCR amplification of only the differentially expressed sequences which were then ligated into T-tailed pBluescript (Hadjeb, N and Berkowitz, GA, *BioTechniques* 20:20-22 1996), allowing for a blue/white selection of cells containing vector with inserts. White cells were isolated and used to obtain plasmid DNA for sequencing.

cDNA library from human neonatal fibroblasts (HNFF)

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Human neonatal fibroblast cells were grown in culture from explants of human neonatal foreskin and the total RNA extracted from these cells using established protocols. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, California), according to the manufacturer's specifications. A cDNA expression library was then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA library from mouse embryonic skin (MEMS)

Embryonic skin was micro-dissected from day 13 post coitum Balb/c mice. Embryonic skin was washed in phosphate buffered saline and mRNA directly isolated from the tissue using the Quick Prep Micro mRNA purification kit (Pharmacia, Sweden). The mRNA was then used to prepare cDNA libraries as described above for the DEPA library.

30 cDNA library from mouse stem cells (KSCL) and transit amplifying (TRAM) cells

Pelts obtained from 1-2 day post-partum neonatal Balb/c mice were washed and incubated in trypsin (BRL Life Technologies) to separate the epidermis from the dermis. Epidermal tissue was disrupted to disperse cells, which were then resuspended in growth medium and centrifuged over Percoll density gradients prepared according to the manufacturer's protocol (Pharmacia, Sweden). Pelleted cells were labeled using Rhodamine 123 (Bertoncello I, Hodgson GS and Bradley TR, Exp Hematol. 13:999-1006, 1985), and analyzed by flow cytometry (Epics Elite Coulter Cytometry, Hialeah, Florida). Single cell suspensions of rhodamine-labeled murine keratinocytes were then labeled with a cross reactive anti-rat CD29 biotin monoclonal antibody (Pharmingen, San Diego, California; clone Ha2/5). Cells were washed and incubated with anti-mouse CD45 phycoerythrin conjugated monoclonal antibody (Pharmingen; clone 30F11.1, 10ug/ml) followed by labeling with streptavidin spectral red (Southern Biotechnology, Birmingham, Alabama). Sort gates were defined using listmode data to identify four populations: CD29 bright rhodamine dull CD45 negative cells; CD29 bright rhodamine bright CD45 negative cells; CD29 dull rhodamine bright CD45 negative cells; and CD29 dull rhodamine dull CD45 negative cells. Cells were sorted, pelleted and snap frozen prior to storage at -80°C. This protocol was followed multiple times to obtain sufficient cell numbers of each population to prepare cDNA libraries. Skin stem cells and transit amplifying cells are known to express CD29, the integrin β1 chain. CD45, a leukocyte specific antigen, was used as a marker for cells to be excluded in the isolation of skin stem cells and transit amplifying cells. Keratinocyte stem cells expel the rhodamine dye more efficiently than transit amplifying cells. The CD29 bright, rhodamine dull, CD45 negative population (putative keratinocyte stem cells; referred to as KSCL), and the CD29 bright, rhodamine bright, CD45 negative population (keratinocyte transit amplifying cells; referred to as TRAM) were sorted and mRNA was directly isolated from each cell population using the Quick Prep Micro mRNA purification kit (Pharmacia, Sweden). The mRNA was then used to prepare cDNA libraries as described above for the DEPA library.

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cDNA Library from Epithelial Cells (MFSE)

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Skin epidermis was removed from flaky skin fsn -/- mice (The Jackson Laboratory, Bar Harbour, ME), the cells dissociated and the resulting single cell suspension placed in culture. After four passages, the cells were harvested. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, MD), was used to obtain mRNA using a Poly(A)Quik mRNA isolation kit (Stratagene, La Jolla, CA), according to the manufacturer's specifications. A cDNA expression library (referred to as the MFSE library) was then prepared from the mRNA by Reverse Transcriptase synthesis using a Lambda ZAP Express cDNA library synthesis kit (Stratagene, La Jolla, CA).

cDNA Libraries from Human Small Airway Epithelial Cells (HLEA and HLEB)

Human small airway epithelium cells SAEC (Cell line number CC-2547, Clonetics Normal Human Cell Systems, Cambrex Corporation, East Rutherford NJ) transformed with human papilloma virus E6E7 that was infected with the bacterium *Yersinia enterocolitica* (ATCC No. 51871, American Type Culture Collection, Manassas VA) and the long form of the Respiratory Syncytial Virus (RSV, ATCC No. VR26), were used as source of RNA to construct the libraries called HLEA and HLEB. Cells from the twelfth passage of SAEC cells were infected with *Y. enterocolitica* for 2 hours at an initial seed of 12.5 bacteria per cell. The cells were disinfected with gentamycin (100 μ g/ml) for 2 hours and harvested 4 hours after infection. The cells were then infected with RSV at a moiety of infection of 0.7 for 1 hour and incubated for 6 and 24 hours. Cells were harvested and the RNA extracted following standard protocols.

Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, CA), according to the manufacturer's specifications. Two cDNA expression libraries were then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA Library from Epithelial Cells (HNKA)

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The subtracted cDNA library (HNKA) from human natural killer (NK) cells was constructed as follows. A NK library was first constructed using pooled RNA extracted from primary NK cells from multiple donors, stimulated for 4 or 20 hours with IL-2 (10 ng/ml), IL-12 (1 ng/ml), IL-15 (50 ng/ml), interferon alpha (IFN-α; 1,000 U/ml) immobilized anti-CD16 or immobilized anti-NAIL antibody, or from unstimulated cells. RNA was extracted following standard procedures. cDNA was prepared using a TimeSaver kit (Pharmacia, Uppsala, Sweden) following the manufacturer's protocol. The cDNA was ligated to *Bgl*II adaptors and size-selected using cDNA sizing columns (Gibco BRL, Gaithersburg MD). The size-selected NK cDNA was ligated into a pDc 409 vector and transformed into *E. coli* DH105 cells. Single-stranded DNA was prepared from the plasmid library using a helper phage (Stratagene)

A second cDNA library (referred to as FF cDNA library) was constructed using fetal foreskin tissue. RNA was extracted and cDNA prepared following standard protocols. The cDNA was ligated into the plasmid pBluescript following standard protocols. 10 μ g of the FF cDNA library was linearized with the restriction endonuclease *Not*I and used as template to synthesize biotin-labeled cRNA using SP6 polymerase.

The subtracted NK cell library (HNKA) was constructed as follows. The biotinylated FF cRNA was mixed with the NK library, ethanol precipitated and resuspended in $5 \,\mu$ l buffer (50 mM HEPES pH 7.4, 10 mM EDTA, 1.5 M NaCl, 0.2% SDS). After addition of $5 \,\mu$ l formamide and heating to 95° for 1 min, the material was left to hybridize for 24 hours at 42°C. 90 μ l of 10 mM HEPES pH 7.3, 1 mM EDTA and 15 μ l streptavidin was added followed by an incubation for 20 min at 50°C. This step was repeated again after extraction with phenol/chloroform.

To the final extracted aqueous phase, the following were added: NaCl to 0.2 M, 1 μ l glycogen and 2 volumes of ethanol. After an overnight precipitation at -20°C, the DNA was pelleted and resuspended in 10 μ l water. A second round of subtraction was performed as above and the DNA transformed into *E. coli* DH105.

cDNA sequences were obtained by high-throughput sequencing of the cDNA libraries described above using a Perkin Elmer/Applied Biosystems Division Prism 377 sequencer.

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Example 2

CHARACTERIZATION OF ISOLATED CDNA SEQUENCES

The isolated cDNA sequences were compared to sequences in the EMBL DNA database using the computer algorithms FASTA and/or BLASTN. The corresponding protein sequences (DNA translated to protein in each of 6 reading frames) were compared to sequences in the SwissProt database using the computer algorithms FASTX and/or BLASTX. Comparisons of DNA sequences provided in SEQ ID NO: 1-119 to sequences in the EMBL DNA database (using FASTA) and amino acid sequences provided in SEQ ID NO: 120-197 to sequences in the SwissProt database (using FASTX) were made as of March 21, 1998. Comparisons of DNA sequences provided in SEQ ID NO: 198-274 to sequences in the EMBL DNA database (using BLASTN) and amino acid sequences provided in SEQ ID NO: 275-348 to sequences in the SwissProt database (using BLASTP) were made as of October 7, 1998. Comparisons of DNA sequences provided in SEQ ID NO: 349-372 to sequences in the EMBL DNA database (using BLASTN) and amino acid sequences provided in SEQ ID NO: 373-398 to sequences in the SwissProt database (using BLASTP) were made as of January 23, 1999. Comparisons of polynucleotide sequences provided in SEQ ID NO: 418-455 and 466-487 to sequences in the EMBL DNA database (using BLASTN) and polypeptide sequences provided in SEQ ID NO: 456-463 and 488-509 to sequences in the SwissProt database (using BLASTP) were made as of April 23, 2000. Comparisons of polynucleotide sequences provided in SEQ ID NO: 510 and 511 to sequences in the EMBL DNA database (using BLASTN) and polypeptide sequences provided in SEQ ID NO: 512 and 513 to sequences in the SwissProt database (using BLASTP) were made as of July 11, 2000. Comparisons of polynucleotide sequences provided in SEQ ID NO: 514-623 to

sequences in the EMBL66 - HTGs + ENSEMBL (May 1, 2001) DNA database (using BLASTN) and polypeptide sequences provided in SEQ ID NO: 624-725 to sequences in the SP_TR_NRDB + ENSEMBL (April 30, 2001) database (using BLASTP) were made as of May 16, 2001.

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Isolated cDNA sequences and their corresponding polypeptide sequences were computer analyzed for the presence of signal sequences identifying secreted molecules. Isolated cDNA sequences that have a signal sequence at a putative start site within the sequence are provided in SEQ ID NO: 1-44, 198-238, 349-358, 399, 418-434, 440-449 and 466-471, 516, 519, 520, 523-527, 531, 532, 535-537, 548, 555, 574-580, 585-587, 589, 593, 595, 596, 598-601, 605-607, 609, 612, 613, 615, 616 and 622. The cDNA sequences of SEQ ID NO: 1-6, 198-199, 349-352, 354, 356-358,419-428, 430-433, 440-444, 446-448, 466, 468-470, 519, 520, 523, 524, 529, 531, 532, 535-537, 579, 585, 587, 598, 605, 609, 613 and 622 were determined to have less than 75% identity (determined as described above), to sequences in the EMBL database using the computer algorithms FASTA or BLASTN, as described above. The polypeptide sequences of SEQ ID NO: 120-125, 275-276, 373-380, 382, 456, 457, 460-462, 488-493, 633, 637, 642, 683, 685, 691, 693, 703, 706, 710, 714, 717, 718, 720, 721 and 725 were determined to have less than 75% identity (determined as described above) to sequences in the SwissProt database using the computer algorithms FASTX or BLASTP, as described above.

Further sequencing of some of the isolated partial cDNA sequences resulted in the isolation of the full-length cDNA sequences provided in SEQ ID NOS: 7-14, 200-231, 372, 418-422, 441-448, 514, 516, 557-561, 567, 568, 619 and 621. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 7-14, 200-231, 372, 514, 516, 557-561, 567, 568, 619 and 621 are provided in SEQ ID NOS: 126-133, 277-308, 396,624, 626, 666-669, 674 and 724 respectively. The cDNA sequences of SEQ ID NO: 418-422 encode the same amino acid sequences as the cDNA sequences of SEQ ID NO: 7 and 11-14, namely SEQ ID NO: 126 and 130-133, respectively. Comparison of the full-

length cDNA sequences with those in the EMBL database using the computer algorithm FASTA or BLASTN, as described above, revealed less than 75% identity (determined as described above) to known sequences, except for the polynucleotides in SEQ ID NOS: 516, 560 and 619. Comparison of the amino acid sequences provided in SEQ ID NOS: 126-133, 277-308, 666, 668, 669 and 724 with those in the SwissProt database using the computer algorithms FASTX or BLASTP, as described above, revealed less than 75% identity (determined as described above) to known sequences.

Comparison of the polypeptide sequences corresponding to the cDNA sequences of SEQ ID NOS: 15-23 with those in the EMBL database using the computer algorithm FASTA database showed less than 75% identity (determined as described above) to known sequences. These polypeptide sequences are provided in SEQ ID NOS: 134-142.

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Further sequencing of some of the isolated partial cDNA sequences resulted in the isolation of full-length cDNA sequences provided in SEQ ID NOS: 24-44, 232-238, 423-434, 449, 466, 468-470, 475, 476 and 484. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 24-44, 232-238, 429, 466, 468-470, 475, 476 and 484 are provided in SEQ ID NOS: 143-163, 309-315, 456, 488, 490-492, 497, 498 and 506, respectively. The cDNA sequences of SEQ ID NO: 423-428, 430-434 and 449 encode the same polypeptide sequences as the cDNA sequences of SEQ ID NO: 27-29, 34, 35, 37, 40-44 and 238, namely SEQ ID NO: 146-148, 153, 154, 156, 159-163 and 315, respectively. These polypeptide sequences were determined to have less than 75% identity, determined as described above to known sequences in the SwissProt database using the computer algorithm FASTX.

Isolated cDNA sequences having less than 75% identity to known expressed sequence tags (ESTs) or to other DNA sequences in the public database, or whose corresponding polypeptide sequence showed less than 75% identity to known protein sequences, were computer analyzed for the presence of transmembrane domains coding for putative membrane-bound molecules. Isolated cDNA sequences that have one or more transmembrane domain(s) within the sequence are provided in SEQ ID NOS: 45-63, 239-253, 359-364, 400-402, 435, 436, 450-452, 455, 470-472, 542, 553-555, 573,

576, 581, 592, 593, 595 and 606. The cDNA sequences of SEQ ID NOS: 45-48, 239-249, 359-361, 363, 450, 451, 455, 472, 473, 553-555, 573, 576 and 592 were found to have less than 75% identity (determined as described above) to sequences in the EMBL database, using the FASTA or BLASTN computer algorithms. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 45-48, 239-249, 359-361, 363, 450, 451, 472, 473, 553-555, 573 and 606 (provided in SEQ ID NOS: 164-167, 316-326, 383, 385-388, 407-408, 460, 461, 494, 495, 662, 663, 664, 679, 682 and 711 respectively) were found to have less than 75% identity, determined as described above, to sequences in the SwissProt database using the FASTX or BLASTP database. The cDNA sequence of SEQ ID NO: 455 encodes the same polypeptide sequence as the cDNA sequence of SEQ ID NO: 359, namely SEQ ID NO: 383.

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Comparison of the polypeptide sequences corresponding to the cDNA sequences of SEQ ID NOS: 49-63, 250-253, 436 and 452 with those in the SwissProt database showed less than 75% identity (determined as described above) to known sequences. These polypeptide sequences are provided in SEQ ID NOS: 168-182, 327-330, 457 and 462, respectively.

Using automated search programs to screen against sequences coding for molecules reported to be of therapeutic and/or diagnostic use, some of the cDNA sequences isolated as described above in Example 1 were determined to encode polypeptides that are family members of known protein families. A family member is here defined to have at least 25% identity in the translated polypeptide to a known protein or member of a protein family. These cDNA sequences are provided in SEQ ID NOS: 64-76, 254-264, 365-369, 403, 437-439, 453, 454, 475-487, 510, 511, 514-527, 529-531, 533-536, 538-546, 548, 549, 553-559, 562, 564, 565, 567, 569-575, 577-589, 591-602, 604-612, 616-618, 621 and 622. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 64-76, 254-264, 365-369, 403, 438, 439, 453, 475-487, 510 and 511, 514-527, 529-531, 533-536, 538-546, 548, 549, 553-559, 562, 564, 565, 567, 569-575, 577-589, 591-602, 604-612, 616-618, 621 and 622 are provided in SEQ ID NOS: 183-195, 331-341, 389-393, 409, 458, 459, 463, 497-509, 624-637, 639-641, 643-

646, 648-656, 658, 659, 662-668, 670, 672-681, 683-707, 709-717 and 721-725, respectively. The cDNA sequences of SEQ ID NO: 437 and 454 encode the same amino acid sequences as the cDNA sequences of SEQ ID NO: 68 and 262, namely SEQ ID NO: 187 and 339, respectively. The cDNA sequences of SEQ ID NOS: 64-68, 254-264, 365-369, 437-439, 453, 454, 475-478, 480-482, 484, 485, 487, 511, 514, 515, 517-520, 522, 523, 525, 529-531, 535, 536, 538, 541, 544-546, 549, 553-559, 564, 565, 567, 569-573, 579, 587, 588, 592, 597, 598, 602, 604, 605, 608-611, 617, 621 and 622 show less than 75% identity (determined as described above) to sequences in the EMBL database using the FASTA or BLASTN computer algorithms. Similarly, the amino acid sequences of SEQ ID NOS: 183-195, 331-341, 389-393, 458, 459, 463, 497, 498, 503-505, 507-509, 512, 513, 628, 632, 633, 637, 640, 655, 662-666, 668, 672, 673, 676, 679, 683, 685, 688, 691, 693, 694, 702, 703, 706, 707, 710, 711, 713, 714, 717, 721, 722 and 725 show less than 75% identity to sequences in the SwissProt database.

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The isolated cDNA sequences encode proteins that influence the growth, differentiation and activation of several cell types, and that may usefully be developed as agents for the treatment and diagnosis of skin wounds, cancers, growth and developmental defects, and inflammatory disease. The utility for certain of the proteins of the present invention, based on similarity to known proteins, is provided in Table 2 below, together with the location of signal peptides and transmembrane domains for certain of the inventive sequences:

Table 2
FUNCTIONS OF NOVEL PROTEINS

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
64, 372	183, 396	Slit, a secreted molecule required for central nervous system development
65	184	Immunoglobulin receptor family. About 40% of leucocyte membrane polypeptides contain immunoglobulin superfamily domains

P/N	A/A SEQ.	
SEQ ID	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
NO:	ID NO.	SHVILLARGIT TO KINOWIN TROTELING, POINCTION
	185,	RIP protein kinase, a serine/threonine kinase that contains a
66,	409	death domain to mediate apoptosis
403		death domain to mediate apoptosis
510	512	Every collular matrix with anidament arough factor demain
67	186	Extracellular protein with epidermal growth factor domain capable of stimulating fibroblast proliferation
60	187	Transforming growth factor alpha, a protein which binds
68, 437	107	epidermal growth factor receptor and stimulates growth and
437		mobility of keratinocytes
69	188	DRS protein which has a secretion signal component and
09	100	whose expression is suppressed in cells transformed by
		oncogenes
70	189	A33 receptor with immunoglobulin-like domains and is
/0	109	expressed in greater than 95% of colon tumors
71	190	Interleukin-12 alpha subunit, component of a cytokine that
/1	190	is important in the immune defense against intracellular
Į	ļ	pathogens. IL-12 also stimulates proliferation and
1		differentiation of TH1 subset of lymphocytes
70	101	Tumor Necrosis Factor receptor family of proteins that are
72	191	involved in the proliferation, differentiation and death of
]		1 · · · · · · · · · · · · · · · · · · ·
73	192	many cell types including B and T lymphocytes. Epidermal growth factor family proteins which stimulate
//3	192	growth and mobility of keratinocytes and epithelial cells.
		EGF is involved in wound healing. It also inhibits gastric
1		acid secretion.
74	193	Fibronectin Type III receptor family. The fibronectin III
/4	193	domains are found on the extracellular regions of cytokine
	}	receptors ·
75	194	Serine/threonine kinases (STK2_HUMAN) which
13	194	participate in cell cycle progression and signal transduction
76	195	Immunoglobulin receptor family
		Receptor with immunoglobulin-like domains and homology
254	331	to A33 receptor which is expressed in greater than 95% of
,		
255	222	colon tumors Epidermal growth factor family proteins which stimulate
255	332	growth and mobility of keratinocytes and epithelial cells.
	1	EGF is involved in wound healing. It also inhibits gastric
1		acid secretion.
256	333	Serine/threonine kinases (STK2_HUMAN) which
256	333	participate in cell cycle progression and signal transduction
L	ــــــــــــــــــــــــــــــــــــــ	barneibare in cen chere brogression and signar manaduction

P/N	A/A SEQ.	
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
- 257	334	Contains protein kinase and ankyrin domains. Possible role in cellular growth and differentiation.
258	335	Notch family proteins which are receptors involved in cellular differentiation.
259	336	Extracellular protein with epidermal growth factor domain capable of stimulating fibroblast proliferation.
260, 453	337, 463	Fibronectin Type III receptor family. The fibronectin III domains are found on the extracellular regions of cytokine receptors.
261	338	Immunoglobulin receptor family
262	339	ADP/ATP transporter family member containing a calcium binding site.
263	340	Mouse CXC chemokine family members are regulators of epithelial, lymphoid, myeloid, stromal and neuronal cell migration and cancers, agents for the healing of cancers, neuro-degenerative diseases, wound healing, inflammatory autoimmune diseases like psoriasis, asthma, Crohns disease and as agents for the prevention of HIV-1 of leukocytes
264	341	Nucleotide-sugar transporter family member.
365	389	Transforming growth factor betas (TGF-betas) are secreted covalently linked to latent TGF-beta-binding proteins (LTBPs). LTBPs are deposited in the extracellular matrix and play a role in cell growth or differentiation.
366	390	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
367	391	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
368	392	Cell wall protein precursor. Are involved in cellular growth or differentiation.
369	393	HT protein is a secreted glycoprotein with an EGF-like domain. It functions as a modulator of cell growth, death or differentiation.
467	489	Myb proto-oncogene (c-Myb), involved in transcription regulation and activation of transcription

P/N	A/A SEQ.	
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
471	493	Chondroitin sulfotransferase, a member of the HNK-1 sulfotransferase family. These molecules are involved in the pathogenesis of arteriosclerosis, and proliferation of arterial smooth muscle cells during development of arteriosclerosis.
472	494	36 kDa nucleolar protein HNP36, a novel growth factor responsive gene expressed in the pituitary and parathyroid glands
475	497	Zinc protease is a matrix metalloproteinase whose activity is directed against components of the extracellular matrix and play an important role in the growth, metastasis and angiogenesis of tumors.
476	498	Diapophytoene dehydrogenase crtn-like molecule. This molecule is similar to the diapophytoene dehydrogenase crt molecule in a major photosynthesis gene cluster from the bacterium Heliobacillus mobilis
477	499	Protocadherin 3 family member, involved in cell to cell interactions.
478	500	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
479	501	Integrin family member. Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
480	502	Similar to secreted HT Protein, a secreted glycoprotein with an EGF-like domain. It functions as a modulator of cell growth, death or differentiation.
481	503	Agrin family member: Agrin is produced by motoneurons and induces the aggregation of nicotinic acetylcholine receptors.
482	504	Macrophage Scavenger Receptors bind to a variety of polyanionic ligands and display complex binding characteristics. They have been implicated in various macrophage-associated processes, including atherosclerosis.
483	505	Similar to GARP, a member of the family of leucine-rich repeat-containing proteins involved in platelet-endothelium interactions.
484	506	Epidermal growth factor family proteins which stimulate growth and mobility of keratinocytes and epithelial cells. EGF is involved in wound healing. It also inhibits gastric

P/N	A/A SEQ.	HE SAME AND A STATE OF THE SAME AND A
SEQ ID	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
NO:		
	,	acid secretion.
485	507	Colony stimulating growth factor family.
	ļ	
486	508	Cytokine receptors
.00		
407	500	IL17 Receptor to Interleukin 17 (IL17), a T cell derived
487	509	cytokine that may play a role in initiation or maintenance of
	}	the inflammatory response.
438	458	MEGF6, a protein containing multiple EGF-like-domains.
		, , , , , , , , , , , , , , , , , , ,
439	459	Protein kinase family member involved in signal
-137	1.55	transduction.
454		
454)	Peroxisomal calcium-dependent solute carrier, a new member of the mitochondrial transporter superfamily.
	<u> </u>	<u> </u>
511	513	Serine/threonine kinase NEK1 is a NIMA-related protein
	1	kinase that phosphorylates serines and threonines, but also
		possesses tyrosine kinase activity. NEK1 has been implicated in the control of meiosis and belongs to the
		NIMA kinase subfamily.
	624 62	6Homologue isolated from rat dermal papilla of integrin
514		alpha-11/beta-1 that is involved in muscle development and
	1	maintaining integrity of adult muscle and other adult
		tissues. Integrin alpha-11/beta-1 is a receptor for collagen
		and belongs to the integrin alpha chain family.
516	625	This is a secreted molecule isolated from rat dermal papillae
		with a signal peptide at the N-terminus (amino acid residues 1 to 21; nucleotides 42 to 104).
517	626	Homologue isolated from a rat dermal papilla library of
317	020	OASIS (old astrocyte specifically-induced substance) and
		that plays a role in regulation of the response of astrocytes
		to inflammation and trauma of the central nervous system
		(CNS) during gliosis. The OASIS gene encodes a putative
		transcription factor belonging to the cyclic AMP responsive
		element binding protein/activating transcription factor
		(CREB/ATF) gene family (Honma et al., Brain Res. Mol. Brain Res. 69:93-103, 1999).
L	L	Diam Res. 03.70-100, 1777).

	111 070	
P/N	A/A SEQ.	CT CT AND TO
SEQ ID	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
NO:		
519	628	This is a secreted molecule isolated from rat dermal papillae
		with a signal peptide at the N-terminus (amino acid residues
		1 to 24; nucleotides 50 to 121).
520	630	This is a secreted molecule isolated from rat dermal papillae
520	""	with a signal peptide at the N-terminus (amino acid residues
		1 to 35; nucleotides 67 to 171).
523	633	This is a secreted molecule isolated from rat dermal papillae
323	033	with a signal peptide at the N-terminus (amino acid residues
ļ		
		1 to 17; nucleotides 3 to 53).
524	634	This is a secreted molecule isolated from rat dermal papillae
		with a signal peptide at the N-terminus (amino acid residues
·		1 to 20; nucleotides 13 to 72).
525, 534	635, 644	Homologue isolated from a rat dermal papilla library of
}		leucyl-specific aminopeptidase, PILS-AP and that plays role
1		in many physiological processes as a substrate-specific
		peptidase. PILS is a new member of the M1 famile of Zn-
1		dependent aminopeptidases that comprises members of
	Į.	closely related enzymes which are known to be involved in
		a variety of physiologically important processes.
526	636	This is a secreted molecule isolated from rat dermal papillae
320	030	with a signal peptide at the N-terminus (amino acid residues
507	(07	1 to 26; nucleotides 114 to 191).
527	637	This is a secreted molecule isolated from rat dermal papillae
		with a signal peptide at the N-terminus (amino acid residues
<u> </u>	 	1 to 26; nucleotides 23 to 100).
529	639	This is a secreted molecule isolated from rat dermal papillae
1	1	with a signal peptide at the N-terminus (amino acid residues
		1 to 17; nucleotides 37 to 87).
530	640	This is a homologue isolated from a rat dermal papilla
1		library of a maturase that is involved in RNA splicing.
ļ	 	
531	641	This is a secreted molecule isolated from rat dermal papillae
		with a signal peptide at the N-terminus (amino acid residues
	<u> </u>	1 to 17; nucleotides 180 to 230).
532	642	This is a secreted molecule isolated from rat dermal papillae
}		with a signal peptide at the N-terminus (amino acid residues
1	1	1 to 32; nucleotides 245 to 340).
535	645	This is a secreted molecule isolated from rat dermal papillae
		with a signal peptide at the N-terminus (amino acid residues
		1 to 25; nucleotides 188 to 333).
		1 - 10 - 10 , 11 - 11 - 11 - 11 - 11 - 1

P/N	A/A SEQ.	
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
536	646	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 21; nucleotides 185 to 247).
537	647	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 24; nucleotides 129 to 200).
541	651	This is a homologue isolated from a rat dermal papilla library of a hepatoma-derived growth factor (HDGF) that is involved in stimulation of cell proliferation.
542	652	This is a receptor-like molecule isolated from rat dermal papillae with two transmembrane domains (amino acid residues 20 to 40 and 58 to 78.
545	655	This is a homologue isolated from a rat dermal papilla library of Link protein (LP) and that is involved in bone formation. LP plays an essential role in endochondral bone formation by stabilizing the supramolecular assemblies of aggrecan and hyaluronan (Deak et al., Cytogenet. Cell Genet. 87:75-79, 1999).
548	658	This is a homologue isolated from a rat dermal papilla library of thrombospondin (TSP). It is a secreted protein with a signal peptide in amino acid residues 1 to 18 (nucleotides 210 to 263). TSP is an extracellular matrix glycoprotein whose expression has been associated with a variety of cellular processes including growth and embryogenesis (Laherty et al., J. Biol. Chem. 267:3,274-3,281, 1992).
553	662	This is a receptor-like molecule isolated from rat dermal papillae with a transmembrane domain (amino acid residues 434 to 454.
554	663	This is a receptor-like molecule isolated from rat dermal papillae with a transmembrane domain (amino acid residues 546 to 566.
555	664	This is a homologue isolated from a rat dermal papilla library of B7-like mouse GL50 (mGL50). It is a receptor-like molecule with a signal peptide in residues 1 to 24 (nucleotides 149 to 220) and a transmembrane domain in amino acid residues 262 to 282. GL50 is a specific ligand for the ICOS receptor and this interaction functions in lymphocyte costimulation (Ling et al., J. Immunol. 164:1,653-1,657, 2000).

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
557, 558, 561-572	666, 667, 670-678	These molecules are differentially expressed in stem cells but not in mature keratinocytes and are involved in developmental processes. They may be employed for diagnosis of tumors with an immature phenotype.
559	668	This is a homologue isolated from a mouse stem cell library of ABSENT IN MELANOMA 1 protein AIM1 and that can be used for diagnosis of tumours with an immature phenotype. AIM1 is a novel gene whose expression is associated with the experimental reversal of tumorigenicity of human malignant melanoma and belongs to the betagamma-crystallin superfamily (Ray et al., Proc. Natl. Acad. Sci. USA 94:3,229-3,234, 1997)
560	669	Homologue isolated from a mouse stem cell library of endothelin-convertin enzyme 2 (ECE-2) and that can be used for diagnosis of tumours with an immature phenotype. Endothelins (ET) are a family of potent vasoactive peptides that are produced from biologically inactive intermediates, termed big endothelins, via a proteolytic processing at Trp21-Val/Ile22. ECE-2, that produces mature ET-1 from big ET-1 both in vitro and in transfected cells. ECE-2 acts as an intracellular enzyme responsible for the conversion of endogenously synthesized big ET-1 at the trans-Golgi network, where the vesicular fluid is acidified (Emoto and Yanagisawa, J. Biol. Chem. 270:15,262-15,268, 1995).
573	679	Mouse homologue of EGF-like molecule containing mucin-like hormone receptor 2 (EMR2). The isolated molecule contains three transmembrane regions: amino acid residues 20 to 40, 66 to 86 and 92 to 112. The epidermal growth factor (EGF)-TM7 proteins [EMR1 and EMR2, F4/80, and CD97] constitute a recently defined class B GPCR subfamily and are predominantly expressed on leukocytes. These molecules possess N-terminal EGF-like domains coupled to a seven-span transmembrane (7TM) moiety via a mucin-like spacer domain (Lin et al., Genomics 67:188-200, 2000).
574	680	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 238 to 288).
575	681	Mouse homologue of a glucocortocoid-inducible protein GIS5 with a signal peptide at the N-terminus (amino acid

P/N	A/A SEQ.		
SEQ ID	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION	
NO:	1,0.	Similar to a second sec	
110.	 	residues 1 to 17; nucleotides 56-106).	
		icsidues 1 to 17, habitotides 50 100).	
576	682	This is a murine surface receptor-like molecule with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 1179 to 199) and a transmembrane domain (amino acid residues 179 to 199).	
577	683	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 16; nucleotides 55 to 102).	
578	684	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 22; nucleotides 12 to 77).	
579	685	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 82 to 132).	
580	686	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 20; nucleotides 20 to 79).	
581	687	This is a murine receptor-like molecule with transmembrane domains at amino acid residues 50 to 70; 84 to 104; 116 to 136 and 179 to 198.	
585	691	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 20; nucleotides 260 to 319).	
586	695	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 22; nucleotides 295 to 360).	
587	693	This is a mouse homologue of serotransferrin, also known as siderophilin or beta-1-metal binding globulin) and that is involved in iron transport. This homologue is a secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 19; nucleotides 43 to 99). Transferrins are iron binding transport proteins which can bind two atoms of ferric iron in association with the binding of an anion, usually bicarbonate. It is responsible for the transport of iron from sites of absorption and heme degradation to those of storage and utilization. Serum transferrin may also have a further role in stimulating cell proliferation. Transferrin belongs to the transferrin family.	

P/N	A/A SEQ.		
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION	
589	695	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 25; nucleotides 1 to 75).	
. 592	697	This is a murine receptor-like molecule with a transmembrane domain in amino acid residues 52 to 72.	
593	698	Mouse homologue of channel inducing factor (CHIF) that plays a role in ion transport. The mouse homologue has a signal peptide at the N-terminus of the predicted polypeptide (amino acid residues 1 to 20; nucleotides 102 to 161) and a transmembrane domain (amino acid residues 38 to 58). CHIF evokes a potassium channel activity (Attali et al., Proc. Natl. Acad. Sci. USA 92:6092-6096, 1995).	
595	700	Homologue of hyaluronan receptor LYVE-1 that plays a role in hyalyronan uptake. This mouse homologue has the characteristic signal peptide and transmembrane domain of a receptor. A signal peptide was identified in the isolated molecule in amino acid residues 1 to 18 (nucleotides 62 to 115) and the transmembrane domain in amino acid residues 233 to 253. The extracellular matrix glycosaminoglycan hyaluronan (HA) is an abundant component of skin and mesenchymal tissues where it facilitates cell migration during wound healing, inflammation, and embryonic morphogenesis. Both during normal tissue homeostasis and particularly after tissue injury, HA is mobilized from these sites through lymphatic vessels to the lymph nodes where it is degraded before entering the circulation for rapid uptake by the liver. LYVE-1 is a receptor for HA on the lymph vessel wall and plays a role in the transport of HA from tissue to lymph (Banerji et al., J. Cell Biol. 144:789-801,1999).	
596	701	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 21; nucleotides 7 to 69).	
598	703	Homologue of tumor-associated glycoprotein E4 (TAA1 or TAGE4) that belongs to the immunoglobulin superfamily. This molecule has a signal peptide at the N-terminus (amino acid residues 1 to 24; nucleotides 71 to 142) and is therefore a secreted protein.	

	,			
P/N	A/A SEQ.			
SEQ ID	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION		
NO:]			
599	704	Homologue of the LUNX protein, also known as nasopharyngeal carcinoma-related protein, tracheal epithelium enriched protein or plunc, that is expressed in epithelial cells in the airways. It has a signal peptide at the N-terminus (amino acid residues 1 to 19; nucleotides 39 to 95). Expression of LUNX is restricted to the trachea, upper airway, nasopharyngeal epithelium and salivary gland (Bingle and Bingle, Biochim. Biophys. Acta 1493:363-367, 2000).		
600	705	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 23; nucleotides 136 to 204.		
601	706	Homologue of prenylcysteine lyase (EC 4.4.1.18) and that is involved in degradation of prenylated proteins. It has a signal peptide at the N-terminus (amino acid residues 1 to 28; nucleotides 22 to 105). Prenylcysteine lyase is a specific enzyme involved in the final step of prenylcysteine metabolism in mammalian cells. The enzyme does not require NADPH as cofactor for prenylcysteine degradation, thus distinguishing it from cytochrome P450- and flavincontaining monooxygenases that catalyze S-oxidation of thioethers (Zhang et al., J. Biol. Chem. 274:35802-35808, 1999).		
605	710	Homologue of endoplasmin, endoplasmic reticulum protein 99 (ERp99), 94 kDa glucose-regulated protein (GRP94) and polymorphic tumor rejection antigen 1 (gp96). The isolated molecule has a signal peptide at the N-terminus (amino acid residue 1 to 21; nucleotides 1867 to 206). ERp99 is an abundant, conserved transmembrane glycoprotein of the endoplasmic reticulum membrane and homologous to the 90-kDa heat shock protein (hsp90) and the 94-kDa glucose regulated protein (GRP94) (Mazzarella and Green, J. Biol. Chem. 262:8875-8883, 1987).		
606	711	Homologue of PILRalpha, formerly known as inhibitory receptor PIRIIalpha and that is involved in signal transduction in various cellular processes. This molecule contains a signal peptide at the N-terminal end (amino acid residues 1-21 and nucleotides 47 to 139) and a transmembrane domain at amino acid residues 191 to 211. SHP-1-mediated dephosphorylation of protein tyrosine		

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
	·	residues is central to the regulation of several cell signaling pathways. PILRalpha, a novel immunoreceptor tyrosine-based inhibitory motif-bearing protein, recruits SHP-1 upon tyrosine phosphorylation and is paired with the truncated counterpart PILRbeta (Mousseau et al., J. Biol. Chem. 275:4467-4474, 2000).
607	712	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 18; nucleotides 38 to 91.
609	714	Homologue of retinal short-chain dehydrogenase/reductase retSDR2 that plays a role on retinal metabolism. It has a signal peptide at the N-terminus at amino acid residues 1 – 29 (nucleotides 302 to 388). Retinol dehydrogenases (RDH) catalyze the reduction of all-trans-retinal to all-transretinol within the photoreceptor outer segment in the regeneration of bleached visual pigments (Haeseleer et al., J. Biol. Chem. 273:21790-21799, 1998)
612	717	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 22; nucleotides 6 to 71.
613	718	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 25; nucleotides 210 to 284.
615	720	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 16; nucleotides 70 to 117.
616	721	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 18; nucleotides 1 to 54.

The locations of open reading frames (ORFs) within certain of the inventive cDNA sequences are shown in Table 3, below.

Table 3

LOCATION OF OPEN READING FRAMES

5

SEQ ID NO		SEQ ID NO
Polynucleotide	ORF	Polypeptide
514	1-2,067	624
515	2-730	625
516	42-1,772	626
517	1-681	627
. 518	170-416	628
519	50-770	629
520	67-708	630
521	110-613	631
522	41-457	632
523	3-230	633
524	13-573	634
525	64-2,856	635
526	114-599	636
527	23-520	637
528	953-1,138	638
529	37-687	639
530	145-366	640
531	180-1,508	643
532	245-442	642
533	125-595	643
534	64-2,856	644
535	188-727	645
536	185-1,081	646
537	129-308	647
538	32-853	648
539	2-268	649
540	3-875	650
541	284-892	651
542	37-276	652
543	127-1,794	653
544	1-735	654
545	142-939	655
546	51-1,082	656
547	143-328	657
548	210-3,728	658
549	26-1,354	659
551	1,236-1,892	660
552	853-1,178	661

SEQ ID NO		SEQ ID NO
Polynucleotide	ORF	Polypeptide
553	54-1,356	662
554	637-2,244	663
555	149-1,072	664
556	18-449	665
557	275-1,171	666
558	453-1,133	667
559	104-2,449	668
560	463-687	669
562	1-1,107	670
563	2-883	671
564	188-2,902	672
565	3-524	673
567	2,584-3,996	674
569	1-960	675
570	315-599	676
571	1-414	677
572	806-1,912	678
. 573	120-752-	679
574	2381,359	680
575	56-1,456	681
576	13-645	682
577	55-1,323	683
578	12-698	684
579	82-810	685
580	20-586	686
581	65-808	687
582	369-761	688
583	1-769	689
584	164-1,321	690
585	260-1,489	691
586	295-1,131	692
587	43-2,136	. 693
588	1-1,203	694
589	1-525	695
591	1-584	696
592	1-522	697
593	102-368	698
594	1-517	699

SEQ ID NO		SEQ ID NO
Polynucleotide	ORF	Polypeptide
595	62-1,018	700
596	7-282	701
597	1-736	702
598	71-1,297	703
599	39-875	704
600	136-930	705
601	22-1,539	706
602	69-521	707
603	104-448	708
604	1-399	709
605	3,068-5,476	710
606	47-721	711
607	38-439	712
608	1-1,656	713
609	302-1,327	714
610	845-1,447	715
611	975-1,375	716
612	6-272	717
613	210-464	718
614	462-869	719
615	70-459	720
616	1-1,107	721
617	1-349	722
618	93-528	723
621	380-1,033	724
622	43-2,115	725

The cDNA sequences of SEQ ID NO: 514, 515, 516, 557, 558, 559, 560, 561, 567, 568, 619 and 621 are extended sequences of SEQ ID NO: 479, 480, 353, 91, 108, 82, 92, 81, 105, 90, 362 and 360, respectively. SEQ ID NO: 516, 520, 521, 523, 525, 526, 529, 534-536, 541-543, 546, 548, 549, 557, 574, 575, 577-581, 584-587, 589, 593, 595, 596, 598-601, 605, 607, 609, 610, 614, 616 and 622 represent full-length cDNA sequences.

The polynucleotide sequences of SEQ ID NOS: 77-117, 265-267, 404-405 and 557-611 are differentially expressed in either keratinocyte stem cells (KSCL) or in transit amplified cells (TRAM) on the basis of the number of times these sequences exclusively appear in either one of the above two libraries; more than 9 times in one and none in the other (Audic S. and Claverie J-M, *Genome Research*, 7:986-995, 1997). The sequences of SEQ ID NOS: 77-89, 265-267 and 365-369 were determined to have less than 75% identity to sequences in the EMBL database using the computer algorithm FASTA or BLASTN, as described above. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 77-117, 265-267, 404-405 and 557-611 are provided in SEQ ID NOS: 666-718. The amino acid sequences of SEQ ID NOS: 666, 668, 669, 671-673, 675, 676, 679, 682, 683, 685, 688, 690, 691, 693, 694, 702, 703, 706-708, 710, 711, 713 and 714 show less than 75% identity to sequences in the SwissProt database.

The polypeptides encoded by these polynucleotide sequences have utility as markers for identification and isolation of these cell types, and antibodies against these proteins may be usefully employed in the isolation and enrichment of these cells from complex mixtures of cells. Isolated polynucleotides and their corresponding proteins exclusive to the stem cell population can be used as drug targets to cause alterations in regulation of growth and differentiation of skin cells, or in gene targeting to transport specific therapeutic molecules to skin stem cells.

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Example 3

ISOLATION AND CHARACTERIZATION OF THE HUMAN HOMOLOG OF MUTRI

The human homolog of muTR1 (SEQ ID NO: 68), obtained as described above in Example 1, was isolated by screening 50,000 pfu's of an oligo dT primed HeLa cell cDNA library. Plaque lifts, hybridization, and screening were performed using standard molecular biology techniques (Sambrook, J, Fritsch, EF and Maniatis, T, eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor: New York, 1989). The determined cDNA sequence of the isolated human homolog (huTR1) is provided in SEQ ID NO: 118, with the corresponding

polypeptide sequence being provided in SEQ ID NO: 196. The library was screened using an [α ³²P]-dCTP labeled double stranded cDNA probe corresponding to nucleotides 1 to 459 of the coding region within SEQ ID NO: 118.

**The polypeptide sequence of huTR1 has regions similar to Transforming Growth Factor-alpha, indicating that this protein functions like an epidermal growth factor (EGF). EGF family members exist in a functional form as small peptides. Alignment of the functional peptides of the EGF family with SEQ ID NO: 196 revealed that an internal segment of SEQ ID NO: 196 (amino acids 54-104) shows greater than 40% identity to the active peptides of EGF, TGF-alpha and Epiregulin. The active peptides of the EGF family are sufficient for activity and contain several conserved residues critical for the maintenance of this activity. These residues are retained in huTR1. This EGF-like protein will serve to stimulate keratinocyte growth and motility, and to inhibit the growth of epithelial-derived cancer cells. This novel gene and its encoded protein may thus be used as agents for the healing of wounds and regulators of epithelial-derived cancers.

Analysis of RNA transcripts by Northern Blotting

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Northern analysis to determine the size and distribution of mRNA for huTR1 was performed by probing human tissue mRNA blots (Clontech) with a probe comprising nucleotides 93-673 of SEQ ID NO: 118, radioactively labeled with $[\alpha^{32}P]$ -dCTP. Prehybridization, hybridization, washing and probe labeling were performed as described in Sambrook, *et al.*, *Ibid.* mRNA for huTR1 was 3.5-4kb in size and was observed to be most abundant in heart and placenta, with expression at lower levels being observed in spleen, thymus, prostate and ovary (Fig. 1).

The high abundance of mRNA for huTR1 in the heart and placenta indicates a role for huTR1 in the formation or maintenance of blood vessels, as heart and placental tissues have an increased abundance of blood vessels, and therefore endothelial cells, compared to other tissues in the body. This, in turn, demonstrates a role for huTR1 in angiogenesis and vascularization of tumors. This is supported by the ability of

Transforming Growth Factor-alpha and EGF to induce *de novo* development of blood vessels (Schreiber, *et al.*, *Science* 232:1250-1253, 1986) and stimulate DNA synthesis in endothelial cells (Schreiber, *et al.*, *Science* 232:1250-1253, 1986), and their over-expression in a variety of human tumors.

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Purification of muTR1 and huTR1

Polynucleotides 177-329 of muTR1 (SEQ ID NO: 268), encoding amino acids 53-103 of muTR1 (SEQ ID NO: 342), and polynucleotides 208-360 of huTR1 (SEQ ID NO: 269), encoding amino acids 54-104 of huTR1 (SEQ ID NO: 343), were cloned into the bacterial expression vector pProEX HT (BRL Life Technologies), which contains a bacterial leader sequence and N-terminal 6xHistidine tag. These constructs were transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid*.

Starter cultures of these recombinant XL1-Blue *E. coli* were grown overnight at 37°C in Terrific broth containing 100 µg/ml ampicillin. This culture was spun down and used to inoculate 500 ml culture of Terrific broth containing 100 µg/ml ampicillin. Cultures were grown until the OD₅₉₅ of the cells was between 0.4 and 0.8, whereupon IPTG was added to 1 mM. Cells were induced overnight and bacteria were harvested by centrifugation.

Both the polypeptide of muTR1 (SEQ ID NO: 342; referred to as muTR1a) and that of huTR1 (SEQ ID NO: 343; referred to as huTR1a) were expressed in insoluble inclusion bodies. In order to purify the polypeptides muTR1a and huTR1a, bacterial cell pellets were re-suspended in lysis buffer (20 mM Tris-HCl pH 8.0, 10 mM beta mercaptoethanol, 1 mM PMSF). To the lysed cells, 1% NP40 was added and the mix incubated on ice for 10 minutes. Lysates were further disrupted by sonication on ice at 95W for 4 x 15 seconds and then centrifuged for 15 minutes at 14,000 rpm to pellet the inclusion bodies.

The resulting pellet was re-suspended in lysis buffer containing 0.5% w/v CHAPS and sonicated on ice for 5-10 seconds. This mix was stored on ice for 1 hour, centrifuged at 14,000 rpm for 15 minutes at 4 °C and the supernatant discarded. The pellet was once

more re-suspended in lysis buffer containing 0.5% w/v CHAPS, sonicated, centrifuged and the supernatant removed as before. The pellet was re-suspended in solubilizing buffer (6 M Guanidine HCl, 0.5 M NaCl, 20 mM Tris HCl, pH 8.0), sonicated at 95 W for 4 x 15 seconds and then centrifuged for 20 minutes at 14,000 rpm and 4 °C to remove debris. The supernatant was stored at 4 °C until use.

Polypeptides muTR1a and huTR1a were purified by virtue of the N-terminal 6x Histidine tag contained within the bacterial leader sequence, using a Nickel-Chelating Sepharose column (Amersham Pharmacia, Uppsala, Sweden) and following the manufacturer's recommended protocol. In order to refold the proteins once purified, the protein solution was added to 5x its volume of refolding buffer (1 mM EDTA, 1.25 mM reduced glutathione, 0.25 mM oxidised glutathione, 20 mM Tris-HCl, pH 8.0) over a period of 1 hour at 4 °C. The refolding buffer was stirred rapidly during this time, and stirring continued at 4 °C overnight. The refolded proteins were then concentrated by ultrafiltration using standard protocols.

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Biological Activities of Polypeptides muTR1a and huTR1a

muTR1 and huTR1 are novel members of the EGF family, which includes EGF, TGFα, epiregulin and others. These growth factors are known to act as ligands for the EGF receptor. The pathway of EGF receptor activation is well documented. Upon binding of a ligand to the EGF receptor, a cascade of events follows, including the phosphorylation of proteins known as MAP kinases. The phosphorylation of MAP kinase can thus be used as a marker of EGF receptor activation. Monoclonal antibodies exist which recognize the phosphorylated forms of 2 MAP kinase proteins – ERK1 and ERK2.

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In order to examine whether purified polypeptides of muTR1a and huTR1a act as a ligand for the EGF receptor, cells from the human epidermal carcinoma cell line A431 (American Type Culture Collection, No. CRL-1555, Manassas, Virginia) were seeded into 6 well plates, serum starved for 24 hours, and then stimulated with purified muTR1a or huTR1a for 5 minutes in serum free conditions. As a positive control, cells were

stimulated in the same way with 10 to 100 ng/ml TGF-alpha or EGF. As a negative control, cells were stimulated with PBS containing varying amounts of LPS. Cells were immediately lysed and protein concentration of the lysates estimated by Bradford assay. 15 µg of protein from each sample was loaded onto 12% SDS-PAGE gels. The proteins were then transferred to PVDF membrane using standard techniques.

For Western blotting, membranes were incubated in blocking buffer (10mM Tris-HCl, pH 7.6, 100 mM NaCl, 0.1% Tween-20, 5% non-fat milk) for 1 hour at room temperature. Rabbit anti-Active MAP kinase pAb (Promega, Madison, Wisconsin) was added to 50 ng/ml in blocking buffer and incubated overnight at 4 °C. Membranes were washed for 30 mins in blocking buffer minus non-fat milk before being incubated with anti rabbit IgG-HRP antibody, at a 1:3500 dilution in blocking buffer, for 1 hour at room temperature. Membranes were washed for 30 minutes in blocking buffer minus non-fat milk, then once for 5 minutes in blocking buffer minus non-fat milk and 0.1% Tween-20. Membranes were then exposed to ECL reagents for 2 min, and then autoradiographed for 5 to 30 min.

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As shown in Fig. 2, both muTR1a and huTR1a were found to induce the phosphorylation of ERK1 and ERK2 over background levels, indicating that muTR1 and huTR1 act as ligands for a cell surface receptor that activates the MAP kinase signaling pathway, possibly the EGF receptor. As shown in Fig. 11, huTR1a was also demonstrated to induce the phosphorylation of ERK1 and ERK2 in CV1/EBNA kidney epithelial cells in culture, as compared with the negative control. These assays were conducted as described above. This indicates that huTR1a acts as a ligand for a cell surface receptor that activates the MAP kinase signaling pathway, possibly the EGF receptor in HeLa and CV1/EBNA cells.

The ability of muTR1a to stimulate the growth of neonatal foreskin (NF) keratinocytes was determined as follows. NF keratinocytes derived from surgical discards were cultured in KSFM (BRL Life Technologies) supplemented with bovine pituatary extract (BPE) and epidermal growth factor (EGF). The assay was performed in 96 well flat-bottomed plates in 0.1 ml unsupplemented KSFM. MuTR1a, human

transforming growth factor alpha (huTGF α) or PBS-BSA was titrated into the plates and 1 x 10³ NF keratinocytes were added to each well. The plates were incubated for 5 days in an atmosphere of 5% CO₂ at 37⁰C. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 3, both muTR1a and the positive control human TGF α stimulated the growth of NF keratinocytes, whereas the negative control, PBS-BSA, did not.

The ability of muTR1a and huTR1a to stimulate the growth of a transformed human keratinocyte cell line, HaCaT, was determined as follows. The assay was performed in 96 well flat-bottomed plates in 0.1 ml DMEM (BRL Life Technologies) supplemented with 0.2% FCS. MuTR1a, huTR1a and PBS-BSA were titrated into the plates and 1 x10³ HaCaT cells were added to each well. The plates were incubated for 5 days in an atmosphere containing 10% CO₂ at 37⁰C. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 4, both muTR1a and huTR1a stimulated the growth of HaCaT cells, whereas the negative control PBS-BSA did not.

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The ability of muTR1a and huTR1a to inhibit the growth of A431 cells was determined as follows. Polypeptides muTR1a (SEQ ID NO: 342) and huTR1a (SEQ ID NO: 343) and PBS-BSA were titrated as described previously (*J. Cell. Biol.* 93:1-4, 1982), and cell death was determined using the MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). Both muTR1a and huTR1a were found to inhibit the growth of A431 cells, whereas the negative control PBS-BSA did not (Fig. 5).

These results indicate that muTR1 and huTR1 stimulate keratinocyte growth and motility, inhibit the growth of epithelial-derived cancer cells, and play a rolê in angiogenesis and vascularization of tumors. This novel gene and its encoded protein may thus be developed as agents for the healing of wounds, angiogenesis and regulators of epithelial-derived cancers.

Upregulation of huTR1 and mRNA expression

HeLa cells (human cervical adenocarcinoma) were seeded in $10 \, \mathrm{cm}$ dishes at a concentration of 1×10^6 cells per dish. After incubation overnight, media was removed and replaced with media containing $100 \, \mathrm{ng/ml}$ of muTR1, huTR1, huTGF α , or PBS as a negative control. After 18 hours, media was removed and the cells lysed in 2 ml of TRIzol reagent (Gibco BRL Life Technologies, Gaithersburg, Maryland). Total RNA was isolated according to the manufacturer's instructions. To identify mRNA levels of huTR1 from the cDNA samples, 1 μ l of cDNA was used in a standard PCR reaction. After cycling for 30 cycles, 5 μ l of each PCR reaction was removed and separated on a 1.5% agarose gel. Bands were visualized by ethidium bromide staining. As can be seen from Fig. 12, both mouse and human TR1 up-regulate the mRNA levels of huTR1 as compared with cells stimulated with the negative control of PBS. Furthermore, TGF α can also up-regulate the mRNA levels of huTR1.

These results indicate that TR1 is able to sustain its own mRNA expression and subsequent protein expression, and thus is expected to be able to contribute to the progression of diseases such as psoriasis where high levels of cytokine expression are involved in the pathology of the disease. Furthermore, since $TGF\alpha$ can up-regulate the expression of huTR1, the up-regulation of TR1 mRNA may be critical to the mode of action of $TGF\alpha$.

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Serum response element reporter gene assay

The serum response element (SRE) is a promoter element required for the regulation of many cellular immediate-early genes by growth. Studies have demonstrated that the activity of the SRE can be regulated by the MAP kinase signaling pathway. Two cell lines, PC12 (rat pheochromocytoma – neural tumor) and HaCaT (human transformed keratinocytes), containing eight SRE upstream of an SV40 promotor and luciferase reporter gene were developed in-house. 5 x 10³ cells were aliquoted per well of 96 well plate and grown for 24 hours in their respective media. HaCaT SRE cells were grown in 5% fetal bovine serum (FBS) in D-MEM supplemented with 2mM L-glutamine (Sigma,

St. Louis, Missouri), 1mM sodium pyruvate (BRL Life Technologies), 0.77mM L-asparagine (Sigma), 0.2mM arginine (Sigma), 160mM penicillin G (Sigma), 70mM dihydrostreptomycin (Roche Molecular Biochemicals, Basel, Switzerland), and 0.5 mg/ml geneticin (BRL Life Technologies). PC12 SRE cells were grown in 5% fetal bovine serum in Ham F12 media supplemented with 0.4 mg/ml geneticin (BRL Life Technologies). Media was then changed to 0.1% FBS and incubated for a further 24 hours. Cells were then stimulated with a titration of TR1 from 1 µg/ml. A single dose of basic fibroblast growth factor at 100 ng/ml (R&D Systems, Minneapolis, Minnesota) or epidermal growth factor at 10 ng/ml (BRL Life Technologies) was used as a positive control. Cells were incubated in the presence of muTR1 or positive control for 6 hours, washed twice in PBS and lysed with 40 μl of lysis buffer (Promega). 10 μl was transferred to a 96 well plate and 10 µl of luciferase substrate (Promega) added by direct injection into each well by a Victor² fluorimeter (Wallac), the plate was shaken and the luminescence for each well read at 3x1 sec Intervals. Fold induction of SRE was calculated using the following equation: Fold induction of SRE = Mean relative luminescence of agonist/Mean relative luminescence of negative control.

As shown in Fig. 13, muTR1 activated the SRE in both PC-12 (Fig. 13A) and HaCaT (Fig. 13B) cells. This indicates that HaCaT and PC-12 cells are able to respond to muTR1 protein and elicit a response. In the case of HaCaT cells, this is a growth response. In the case of PC-12 cells, this may be a growth, a growth inhibition, differentiation, or migration response. Thus, TR1 may be important in the development of neural cells or their differentiation into specific neural subsets. TR1 may also be important in the development and progression of neural tumors.

Inhibition by the EGF receptor assay

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The HaCaT growth assay was conducted as previously described, with the following modifications. Concurrently with the addition of EGF and TR1 to the media, anti-EGF Receptor (EGFR) antibody (Promega, Madison, Wisconsin) or the negative

control antibody, mouse IgG (PharMingen, San Diego, California), were added at a concentration of 62.5 ng/ml.

As seen in Fig. 14, an antibody which blocks the function of the EGFR inhibited the mitogenicity of TR1 on HaCaT cells. This indicates that the EGFR is crucial for transmission of the TR1 mitogenic signal on HaCaT cells. TR1 may bind directly to the EGF receptor. TR1 may also bind to any other members of the EGFR family (for example, ErbB-2, -3, and/or -4) that are capable of heterodimerizing with the EGFR.

Splice variants of huTR1

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A variant of huTR1 was isolated from the same library as huTR1, following the same protocols. The sequence referred to as huTR1-1 (also known as TR1δ) is a splice variant of huTR1 and consists of the ORF of huTR1 minus amino acids 15 to 44 and 87 to 137. These deletions have the effect of deleting part of the signal sequence and following amino terminal linker sequence, residues following the second cysteine residue of the EGF motif and the following transmembrane domain. However, cysteine residue 147 (huTR1 ORF numbering) may replace the deleted cysteine and thus the disulphide bridges are likely not affected. Therefore, huTR1-1 is an intracellular form of huTR1. It functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGFα. The determined nucleotide sequence of huTR1-1, is given in SEQ ID NO: 412, with the corresponding amino acid sequence being provided in SEQ ID NO: 415.

Four additional splice variants of huTr1 were isolated by PCR on first strand cDNA made from RNA isolated from HeLa cells by standard protocols. These splice variants of huTR1 are referred to as TR1-2 (also known as TR1 β), TR1-3 (also known as TR1 γ), TR1 ϵ and TR1 ϕ .

TR1-2 consists of the ORF of huTR1 minus amino acids 95 to 137. This deletion has the effect of deleting the transmembrane domain. Therefore TR1-2 is a secreted form of huTR1 and binds with equal or greater affinity to the TR1 receptor as huTR1, since the EGF domain remains intact. It functions as an agonist or an antagonist to huTR1 or other

EGF family members, including EGF and TGFα. The determined cDNA sequence of TR1-2 is given in SEQ ID NO: 410 and the corresponding amino acid sequence in SEQ ID NO: 413.

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TR1-3 consists of the ORF of huTR1 minus amino acids 36 to 44 and amino acids 86 to 136. These deletions have the effect of deleting part of the amino terminal linker sequence, residues following the second cysteine of the EGF motif and the following transmembrane domain. However, cysteine residue 147 (huTR1 ORF numbering) may replace the deleted cysteine and thus the disulphide bridges are likely not affected. Therefore, TR1-3 is also a secreted form of huTR1 and functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGF α . The determined cDNA sequence of TR1-3 is given in SEQ ID NO: 411 and the corresponding amino acid sequence is SEQ ID NO: 414.

TR1ε consists of the ORF of huTR1 minus amino acids 86 to 136. This deletion has the effect of deleting residues following the second cysteine of the EGF motif and the transmembrane domain. However, cysteine residue 147 (huTR1 ORF numbering) may replace the deleted cysteine and thus the disulphide bridges are likely not affected. Therefore, TR1ε is also a secreted form of huTR1 and functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGFα. The determined cDNA sequence of TR1ε is given in SEQ ID NO: 371 and the corresponding polypeptide sequence in SEQ ID NO: 395.

TR1φ consists of the ORF of huTR1 minus amino acids 36 to 44 and amino acids 95 to 136. These deletions have the effect of deleting part of the amino terminal linker sequence and the transmembrane domain. Therefore TR1φ is a secreted form of huTR1 and binds with equal or greater affinity to the TR1 receptor as huTR1, since the EGF domain remains intact. It functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGFα. The determined nucleotide sequence of TR1φ is given in SEQ ID NO: 416 and the corresponding polypeptide sequence in SEQ ID NO: 417.

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Example 4

IDENTIFICATION, ISOLATION AND CHARACTERIZATION OF DP3

A partial cDNA fragment, referred to as DP3, was identified by differential display RT-PCR (modified from Liang P and Pardee AB, *Science* 257:967-971, 1992) using mRNA from cultured rat dermal papilla and footpad fibroblast cells, isolated by standard cell biology techniques. This double stranded cDNA was labeled with [α³²P]-dCTP and used to identify a full length DP3 clone by screening 400,000 pfu's of an oligo dT-primed rat dermal papilla cDNA library. The determined full-length cDNA sequence for DP3 is provided in SEQ ID NO: 119, with the corresponding amino acid sequence being provided in SEQ ID NO: 197. Plaque lifts, hybridization and screening were performed using standard molecular biology techniques.

Example 5 ISOLATION AND CHARACTERIZATION OF KS1

Analysis of RNA transcripts by Northern Blotting

Northern analysis to determine the size and distribution of mRNA for muKS1 (SEQ ID NO: 263) was performed by probing murine tissue mRNA blots with a probe consisting of nucleotides 268-499 of muKS1, radioactively labeled with $[\alpha^{32}P]$ -dCTP. Prehybridization, hybridization, washing, and probe labeling were performed as

described in Sambrook, et al., Ibid. mRNA for muKS1 was 1.6 kb in size and was observed to be most abundant in brain, lung, or any muscle, and heart. Expression could also be detected in lower intestine, skin, bone marrow, and kidney. No detectable signal was found in testis, spleen, liver, thymus, stomach.

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Human homologue of muKS1

MuKS1 (SEQ ID NO: 263) was used to search the EMBL database (Release 50, plus updates to June, 1998) to identify human EST homologues. The top three homologies were to the following ESTs: accession numbers AA643952, HS1301003 and AA865643. These showed 92.63% identity over 285 nucleotides, 93.64% over 283 nucleotides and 94.035% over 285 nucleotides, respectively. Frame shifts were identified in AA643952 and HS1301003 when translated. Combination of all three ESTs identified huKS1 (SEQ ID NO: 270) and translated polypeptide SEQ ID NO: 344. Alignment of muKS1 and huKS1 polypeptides indicated 95% identity over 96 amino acids.

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Identification of KSCL009274 cDNA sequence

A directionally cloned cDNA library was constructed from immature murine keratinocytes and submitted for high-throughput sequencing. Sequence data from a clone designated KDCL009274 showed 35% identity over 72 amino acids with rat macrophage inflammatory protein-2B (MIP-2B) and 32% identity over 72 amino acids with its murine homologue. The insert of 1633bp (SEQ ID NO: 464; Fig. 15A) contained an open reading frame of 300bp with a 5' untranslated region of 202bp and a 3' untranslated region of 1161bp. A poly-adenylation signal of AATAAA is present 19 base pairs upstream of the poly-A tail. The mature polypeptide (SEQ ID NO: 465) is 77 amino acids in length containing 4 conserved cysteines with no ELR motif. The putative signal peptide cleavage site beween GLY 22 and Ser 23 was predicted by the hydrophobicity profile. This putative chemokine was identical to KS1. The full length sequence was screened against the EMBL database using the BLAST program and showed some identity at the nucleotide level with human EST clones AA643952, AA865643, and

HS1301003, respectively. A recently described human CXC chemokine, BRAK, has some identity with KS1 at the protein level. The alignment of KS1 (referred to in Fig. 15B as KLF-1), BRAK, and other murine α -chemokines is shown in Fig. 15B. The phylogenetic relationship between KS1 and other α -chemokine family members was determiend using the Phylip program. KS1 and BRAK demonstrate a high degree of divergence from the other α -chemokines, supporting the relatively low homology shown in the multiple alignment.

Bacterial expression and purification of muKS1 and huKS1

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Polynucleotides 269-502 of muKS1 (SEQ ID NO: 271), encoding amino acids 23-99 of polypeptide muKS1 (SEQ ID NO: 345), and polynucleotides 55-288 of huKS1 (SEQ ID NO: 272), encoding amino acids 19-95 of polypeptide huKS1 (SEQ ID NO: 346), were cloned into the bacterial expression vector pET-16b (Novagen, Madison, Wisconsin), which contains a bacterial leader sequence and N-terminal 6xHistidine tag. These constructs were transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid*.

Starter cultures of recombinant BL 21 (DE3) *E. coli* (Novagen) containing SEQ ID NO: 271 (muKS1a) and SEQ ID NO: 272 (huKS1a) were grown in NZY broth containing 100 μg/ml ampicillin (Gibco-BRL Life Technologies) at 37°C. Cultures were spun down and used to inoculate 800 ml of NZY broth and 100 μg/ml ampicillin. Cultures were grown until the OD₅₉₅ of the cells was between 0.4 and 0.8. Bacterial expression was induced for 3 hours with 1 mM IPTG. Bacterial expression produced an induced band of approximately 15kDa for muKS1a and huKS1a.

MuKS1a and huKS1a were expressed in insoluble inclusion bodies. In order to purify the polypeptides, bacterial cell pellets were re-suspended in lysis buffer (20 mM Tris-HCl pH 8.0, 10 mM βMercaptoethanol, 1 mM PMSF). To the lysed cells, 1% NP-40 was added and the mix incubated on ice for 10 minutes. Lysates were further disrupted by sonication on ice at 95 W for 4 x 15 seconds and then centrifuged for 10 minutes at 18,000 rpm to pellet the inclusion bodies.

The pellet containing the inclusion bodies was re-suspended in lysis buffer containing 0.5% w/v CHAPS and sonicated for 5-10 seconds. This mix was stored on ice for 1 hour, centrifuged at 14000 rpm for 15 minutes at 4°C and the supernatant discarded. The pellet was once more re-suspended in lysis buffer containing 0.5% w/v CHAPS, sonicated, centrifuged, and the supernatant removed as before. The pellet was resuspended in solubilizing buffer (6 M guanidine HCl, 0.5 M NaCl, 20 mM Tris-HCl pH 8.0), sonicated at 95W for 4 x 15 seconds and centrifuged for 10 minutes at 18000 rpm and 4°C to remove debris. The supernatant was stored at 4°C. MuKS1a and huKS1a were purified by virtue of the N-terminal 6x histidine tag contained within the bacterial leader sequence, using a Nickel-Chelating sepharose column (Amersham Pharmacia, Uppsala, Sweden) and following the manufacturer's protocol. Proteins were purified twice over the column to reduce endotoxin contamination. In order to re-fold the proteins once purified, the protein solution was dialysed in a 4 M-2 M urea gradient in 20 mM tris-HCl pH 7.5 + 10% glycerol overnight at 4°C. The protein was then further dialysed 2x against 2 litres of 20 mM Tris-HCl pH 7.5 + 10% (w/v) glycerol. Preparations obtained were greater than 95% pure as determined by SDS-PAGE. Endotoxin contamination of purified proteins were determined using a limulus amebocyte lysate assay kit (BIO Whittaker, Walkersville, MD). Endotoxin levels were <0.1 ng/µg of protein. Internal amino acid sequencing was performed on tryptic peptides of KS1.

An Fc fusion protein was produced by expression in HEK 293 T cells. 35µg of KLF-1plGFc DNA to transfect 6 x 10⁶ cells per flask, 200 mls of Fc containing supernatant was produced. The Fc fusion protein was isolated by chromatography using an Affiprep protein A resin (0.3 ml column, Biorad). After loading, the column was washed with 15 mls of PBS, followed by a 5 ml wash of 50 mM Na citrate pH 5.0. The protein was then eluted with 6 column volumes of 50 mM Na citrate pH 2.5, collecting 0.3 ml fractions in tubes containing 60µl of 2M Tris-HCI pH 8.0. Fractions were analyzed by SDS-PAGE.

Peptide sequencing of muKS1 and huKS1

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Bacterially expressed muKS1 and huKS1 were separated on polyacrylamide gels and induced bands of 15 kDa were identified. The predicted size of muKS1 is 9.4 kDa. To obtain the amino acid sequence of the 15 kDa bands, 20 µg recombinant muKS1 and huSK1 was resolved by SDS-PAGE and electroblotted onto Immobilon PVDF membrane (Millipore, Bedford, Massachusetts). Internal amino acid sequencing was performed on tryptic peptides of muKS1 and huKS1 by the Protein Sequencing Unit at the University of Auckland, New Zealand.

The determined amino acid sequences for muKS1 and huKS1 are given in SEQ ID NOS: 397 and 398, respectively. These amino acid sequences confirmed that the determined sequences are identical to those established on the basis of the cDNA sequences. The size discrepancy has previously been reported for other chemokines (Richmond A, Balentien E, Thomas HG, Flaggs G, Barton DE, Spiess J, Bordoni R, Francke U, Derynck R, "Molecular characterization and chromosomal mapping of melanoma growth stimulatory activity, a growth factor structurally related to beta-thromboglobulin," *EMBO J.* 7:2025-2033, 1988; Liao F, Rabin RL, Yannelli JR, Koniaris LG, Vanguri P, Farber JM, "Human Nig chemokine: biochemical and functional characterization," *J. Exp. Med.* 182:1301-1314, 1995). The isoelectric focusing point of these proteins was predicted to be 10.26 using DNASIS (HITACHI Software Engineering, San Francisco, California). Recombinant Fc tagged KS1 expresssed and purified using protein A affinity column chromatography revealed a homogenous protein with a molecular mass of 42kDa.

Oxidative burst assay

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Oxidative burst assays were used to determine responding cell types. 1×10^7 PBMC cells were resuspended in 5 ml HBSS, 20mM HEPES, 0.5% BSA and incubated for 30 minutes at 37°C with 5 μ l 5 mM dichloro-dihydrofluorescein diacetate (H₂DCFDA, Molecular Probes, Eugene, Oregon). 2×10^5 H₂DCFDA-labeled cells were loaded in each well of a flat-bottomed 96 well plate. 10μ l of each agonist was added simultaneously into the well of the flat-bottomed plate to give final concentrations of 100 ng/ml (fMLP was used at 10μ M). The plate was then read on a Victor² 1420

multilabel counter (Wallac, Turku, Finland) with a 485 nm excitation wavelength and 535 nm emission wavelength. Relative fluorescence was measured at 5 minute intervals over 60 minutes.

A pronounced respiratory burst was identified in PBMC with a 2.5 fold difference between control treated cells (TR1) and cells treated with 100 ng/ml muKS1 (Fig. 8). Human stromal derived factor- 1α (SDF1 α) (100 ng/ml) and 10 μ M formyl-Met-Leu-Phe (fMLP) were used as positive controls.

Chemotaxis assay

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Cell migration in response to muKS1 was tested using a 48 well Boyden's chamber (Neuro Probe Inc., Cabin John, Maryland) as described in the manufacturer's protocol. In brief, agonists were diluted in HBSS, 20mM HEPES, 0.5% BSA and added to the bottom wells of the chemotactic chamber. THP-1 cells were re-suspended in the same buffer at 3 x 10⁵ cells per 50 µ1. Top and bottom wells were separated by a PVP-free polycarbonate filter with a 5 µm pore size for monocytes or 3 µm pore size for lymphocytes. Cells were added to the top well and the chamber incubated for 2 hours for monocytes and 4 hours for lymphocytes in a 5% CO₂ humidified incubator at 37°C. After incubation, the filter was fixed and cells scraped from the upper surface. The filter was then stained with Diff-Quick (Dade International Inc., Miami, Florida) and the number of migrating cells counted in five randomly selected high power fields. The results are expressed as a migration index (the number of test migrated cells divided by the number of control migrated cells).

Using this assay, muKS1 was tested against T cells and THP-1 cells. MuKS1 induced a titrateable chemotactic effect on THP-1 cells from 0.01 ng/ml to 100 ng/ml (Fig. 9). Human SDF1α was used as a positive control and gave an equivalent migration. MuKS1 was also tested against IL-2 activated T cells. However, no migration was evidence for muKS1 even at high concentrations, whereas SDF-1α provided an obvious titrateable chemotactic stimulus. Therefore, muKS1 appears to be chemotactic for THP-1 cells but not for IL-2 activated T cells at the concentrations tested.

Flow cytometric binding studies

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Binding of KLF-1 to THP-1 and Jurkat cells was tested in the following manner. THP-1 or Jurkat cells (5 x 10⁶) were resuspended in 3 mls of wash buffer (2% FBS and 0.2% sodium azide in PBS) and pelleted at 4°C, 200 x g for 5 minutes. Cells were then blocked with 0.5% mouse and goat sera for 30 minutes on ice. Cells were washed, pelleted, resuspended in 50 µl of KLF-1Fc at 10 µg/ml and incubated for 30 minutes on ice. After incubation, the cells were prepared as before and resuspended in 50 µl of goat anti-human IgG biotin (Southern Biotechnology Associates, AL) at 10 µg/ml and incuated for 30 minutes on ice. Finally, cells were washed, pelleted and resuspended in 50 μl of streptavidin-RPE (Southern Biotechnology Associates, AL) at 10 μg/ml and incuabated for a further 30 minutes on ice in the dark. Cells were washed and resuspended in 250 µl of wash buffer and stained with 1µl of 10 µg/ml propidium iodide (Sigma) to exclude any dead cells. Purified Fc fragment (10 µg/ml) was used as a negative control in place of KLF-1Fc to determine non-specific binding. Ten thousand gated events were analyzed on log scale using PE filter arrangement with peak transmittance at 575 nm and bandwidth of 10 nm on an Elite cell sorter (Coulter Cytometry).

The respiratory burst and migration assays indicated that KS1 is active on monocytes and not T cells; therefore, the KS1 Fc fusion protein was tested in a binding study with THP-1 and Jurkat T cells. KS1 Fc showed a marked positive shift on THP-1 cells compared with the Fc fragment alone. In contrast, KS1 demonstrated no positive binding with Jurkat cells in an identical experiment.

25 Full length sequence of muKS1 clone

The nucleotide sequence of muKS1 was extended by determining the base sequence of additional ESTs. Combination of all the ESTs identified the full-length muKS1 (SEQ ID NO: 370) and the corresponding translated polypeptide sequence in SEQ ID NO: 394.

Analysis of human RNA transcripts by Northern blotting

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Northern blot analysis to determine the size and distribution of mRNA for the human homologue of muKS1 was performed by probing human tissue blots (Clontech, Palo Alto, California) with a radioactively labeled probe consisting of nucleotides 1 to 288 of huKS1 (SEQ ID NO: 270). Prehybridization, hybridization, washing, and probe labeling were performed as described in Sambrook, et al., Ibid. mRNA for huKS1 was 1.6 kb in size and was observed to be most abundance in kidney, liver, colon, small intestine, and spleen. Expression could also be detected in pancreas, skeletal muscle, placenta, brain, heart, prostate, and thymus. No detectable signal was found in lung, ovary, and testis.

Analysis of human RNA transcripts in tumor tissue by Northern blotting

Northern blot analysis to determine distribution of huKS1 in cancer tissue was performed as described previously by probing tumor panel blots (Invitrogen, Carlsbad, California). These blots make a direct comparison between normal and tumor tissue. MRNA was observed in normal uterine and cervical tissue but not in the respective tumor tissue. In contrast, expression was up-regulated in breast tumor and down-regulated in normal breast tissue. No detectable signal was found in either ovary or ovarian tumors.

Injection of bacterially recombinant muKS1 into C3H/HeJ mice

Eighteen C3H/HeJ mice were divided into 3 groups and injected intraperitoneally with muKS1, GV14B, or phosphate buffered saline (PBS). GV14B is a bacterially expressed recombinant protein used as a negative control. Group 1 mice were injected with 50 μg of muKS1 in 1 ml of PBS; Group 2 mice were injected with 50 μg of GV14B in 1 ml of PBS; and Group 3 mice with 1 ml of PBS. After 18 hours, the cells in the peritoneal cavity of the mice were isolated by intraperitoneal lavage with 2 x 4 ml washes with harvest solution (0.02% EDTA in PBS). Viable cells were counted from individual

mice from each group. Mice injected with 50 µg of muKS1 had on average a 3-fold increase in cell numbers (Fig. 10).

20 µg of bacterial recombinant muKS1 was injected subcutaneously into the left hind foot of three C3H/HeJ mice. The same volume of PBS was injected into the same site on the right-hand side of the same animal. After 18 hours, mice were examined for inflammation. All mice showed a red swelling in the foot pad injected with bacterially recombinant KS1. From histology, sites injected with muKS1 had an inflammatory response of a mixed phenotype with mononuclear and polymorphonuclear cells present.

10 Injection of bacterially expressed muKSla into nude mice

To determine whether T cells are required for the inflammatory response, the experiment was repeated using nude mice. Two nude mice were anaesthetised intraperitoneally with 75 µl of 1/10 dilution of Hypnorm (Janssen Pharmaceuticals, Buckinghamshire, England) in phosphate buffered saline. 20ug of bacterially expressed muKS1a (SEQ ID NO: 345) was injected subcutaneously in the left hind foot, ear and left-hand side of the back. The same volume of phosphate buffered saline was injected in the same sites but on the right-hand side of the same animal. Mice were left for 18 hours and then examined for inflammation. Both mice showed a red swelling in the ear and foot sites injected with the bacterially expressed protein. No obvious inflammation could be identified in either back site. Mice were culled and biopsies taken from the ear, back and foot sites and fixed in 3.7% formol saline. Biopsies were embedded, sectioned and stained with Haemotoxylin and eosin. Sites injected with muKS1a had a marked increase in polymorphonuclear granulocytes, whereas sites injected with phosphate buffered saline had a low background infiltrate of polymorphonuclear granulocytes.

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Discussion

Chemokines are a large superfamily of highly basic secreted proteins with a broad number of functions (Baggiolini, et al., Annu. Rev. Immunol., 15:675-705, 1997; Ward, et al., Immunity, 9:1-11, 1998; Horuk, Nature, 393:524-525, 1998). The polypeptide

sequences of muKS1 and huKS1 have similarity to CXC chemokines, suggesting that this protein will act like other CXC chemokines. The in vivo data from nude mice supports this hypothesis. This chemokine-like protein may therefore be expected to stimulate leukocyte, epithelial, stromal, and neuronal cell migration; promote angiogenesis and vascular development; promote neuronal patterning, hemopoietic stem cell mobilization, keratinocyte and epithelial stem cell patterning and development, activation and proliferation of leukocytes; and promotion of migration in wound healing events. It has recently been shown that receptors to chemokines act as co-receptors for HIV-1 infection of CD4+ cells (Cairns, et al., Nature Medicine, 4:563-568, 1998) and that high circulating levels of chemokines can render a degree of immunity to those exposed to the HIV virus (Zagury, et al., Proc. Natl. Acad. Sci. USA 95:3857-3861, 1998). This novel gene and its encoded protein may thus be usefully employed as regulators of epithelial, lymphoid, myeloid, stromal, and neuronal cells migration and cancers; as agents for the treatment of cancers, neuro-degenerative diseases, inflammatory autoimmune diseases such as psoriasis, asthma and Crohn's disease for use in wound healing; and as agents for the prevention of HIV-1 binding and infection of leukocytes.

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We have also shown that muKS1 promotes a quantifiable increase in cell numbers in the peritoneal cavity of C3H/HeJ mice injected with muKS1. Furthermore, we have shown that muKS1 induces an oxidative burst in human peripheral blood mononuclear cells and migration in the human monocyte leukemia cell line, THP-1, suggesting that monocyte/macrophages are one of the responsive cell types for KS1. In addition to this, we demonstrated that huKS1 was expressed at high levels in a number of non-lymphoid tissues, such as the colon and small intestine, and in breast tumors. It was also expressed in normal uterine and cervical tissue, but was completely down-regulated in their respective tumors. It has recently been shown that non-ELR chemokines have demonstrated angiostatic properties. IP-10 and Mig, two non-ELR chemokines, have previously been shown to be up-regulated during regression of tumors (Tannenbaum CS, Tubbs R, Armstrong D, Finke JH, Bukowski RM, Hamilton TA, "The CXC Chemokines IP-10 and Mig are necessary for IL-12-mediated regression of the mouse RENCA

tumor," J. Immunol. 161: 927-932, 1998), with levels of expression inversely correlating with tumor size (Kanegane C, Sgadari C, Kanegane H, Teruya-Feldstine J, Yao O, Gupta G, Farber JM, Liao F, Liu L, Tosato G, "Contribution of the CXC Chemokines IP-10 and Mig to the antitumor effects of IL-12," J. Leuko. Biol. 64: 384-392, 1998). Furthermore, neutralizing antibodies to IP-10 and Mig would reduce the anti-tumor effect, indicating the contribution these molecules make to the anti-tumor effects. Therefore, it is expected that in the case of cervical and uterine tumors, KS1 would have similar properties.

The data demonstrates that KS1 is involved in cell migration showing that one of the responsive cell types is monocyte/macrophage. The human expression data in conjunction with the *in vitro* and *in vivo* biology demonstrates that this molecule may be a useful regulator in cell migration, and as an agent for the treatment of inflammatory diseases, such as Crohn's disease, ulcerative colitis, and rheumatoid arthritis; and cancers, such as cervical adenocarcinoma, uterine leiomyoma, and breast invasive ductal carcinoma.

Example 6

CHARACTERIZATION OF KS2

KS2 contains a transmembrane domain and may function as either a membrane-bound ligand or a receptor. Northern analysis indicated that the mRNA for KS2 was expressed in the mouse keratinocyte cell line, Pam212, consistent with the cDNA being identified in mouse keratinocytes.

Mammalian Expression

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To express KS2, the extracellular domain was fused to the amino terminus of the constant domain of immunoglobulinG (Fc) that had a C-terminal 6xHistidine tag. This was performed by cloning polynucleotides 20-664 of KS2 (SEQ ID NO: 273), encoding amino acids 1-215 of polypeptide KS2 (SEQ ID NO: 347), into the mammalian expression vector pcDNA3 (Invitrogen, NV Leek, Netherlands), to the amino terminus of

the constant domain of immunoglobulinG (Fc) that had a C-terminal 6xHistidine tag. This construct was transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid*. The Fc fusion construct of KS2a was expressed by transfecting Cos-1 cells in 5 x T175 flasks with 180 µg of KS1a using DEAE-dextran. The supernatant was harvested after seven days and passed over a Ni-NTA column. Bound KS2a was eluted from the column and dialysed against PBS.

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The ability of the Fc fusion polypeptide of KS2a to inhibit the IL-2 induced growth of concanavalin A stimulated murine splenocytes was determined as follows. A single cell suspension was prepared from the spleens of BALB/c mice and washed into DMEM (GIBCO-BRL) supplemented with 2 mM L-glutamine, 1 mM sodium pyruvate, 0.77 mM L-asparagine, 0.2 mM L-arganine, 160 mM penicillin G, 70 mM dihydrostreptomycin sulfate, 5 x 10⁻² mM beta mercaptoethanol and 5% FCS (cDMEM). Splenocytes (4 x 10⁶/ml) were stimulated with 2 μg/ml concanavalin A for 24 hrs at 37°C in 10% CO₂. The cells were harvested from the culture, washed 3 times in cDMEM and resuspended in cDMEM supplemented with 10 ng/ml rhuIL-2 at 1 x 10⁵ cells/ml. The assay was performed in 96 well round bottomed plates in 0.2 ml cDMEM. The Fc fusion polypeptide of KS2a, PBS, LPS and BSA were titrated into the plates and 1 x 10⁴ activated T cells (0.1 ml) were added to each well. The plates were incubated for 2 days in an atmosphere containing 10% CO₂ at 37°C. The degree of proliferation was determined by pulsing the cells with 0.25 uCi/ml tritiated thymidine for the final 4 hrs of culture after which the cells were harvested onto glass fiber filtermats and the degree of thymidine incorporation determined by standard liquid scintillation techniques. As shown in Fig. 6, the Fc fusion polypeptide of KS2a was found to inhibit the IL-2 induced growth of concanavalin A stimulated murine splenocytes, whereas the negative controls PBS, BSA and LPS did not.

This data demonstrates that KS2 is expressed in skin keratinocytes and inhibits the growth of cytokine induced splenocytes. This indicates a role for KS2 in the regulation of skin inflammation and malignancy.

Example 7

Characterization of KS3

KS3 encodes a polypeptide of 40 amino acids (SEQ ID NO: 129). KS3 contains a signal sequence of 23 amino acids that would result in a mature polypeptide of 17 amino acids (SEQ ID NO: 348; referred to as KS3a).

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KS3a was prepared synthetically (Chiron Technologies, Victoria, Australia) and observed to enhance transferrin-induced growth of the rat intestinal epithelial cells IEC-18 cells. The assay was performed in 96 well flat-bottomed plates in 0.1 ml DMEM (GIBCO-BRL Life Technologies) supplemented with 0.2% FCS. KS3a (SEQ ID NO: 348), apo-Transferrin, media and PBS-BSA were titrated either alone, with 750 ng/ml Apo-transferrin or with 750 ng/ml BSA, into the plates and 1 x10³ IEC-18 cells were added to each well. The plates were incubated for 5 days at 37°C in an atmosphere containing 10% CO₂. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 7, KS3a plus Apo-transferrin was found to enhance transferrin-induced growth of IEC-18 cells, whereas KS3a alone or PBS-BSA did not, indicating that KS3a and Apo-transferrin act synergistically to induce the growth of IEC-18 cells.

This data indicates that KS3 is epithelial derived and stimulates the growth of epithelial cells of the intestine. This suggests a role for KS3 in wound healing, protection from radiation- or drug-induced intestinal disease, and integrity of the epithelium of the intestine.

SEQ ID NOS: 1-725 are set out in the attached Sequence Listing. The codes for polynucleotide and polypeptide sequences used in the attached Sequence Listing confirm to WIPO Standard ST.25 (1988), Appendix 2.

All references cited herein, including patent references and non-patent references, are hereby incorporated by reference in their entireties.

Although the present invention has been described in terms of specific embodiments, changes and modifications can be carried out without departing from the

scope of the invention which is intended to be limited only by the scope of the appended claims.

We claim:

- 1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of: (a) sequences recited in SEQ ID NOS: 466-487, 510, 511 and 514-623; (b) complements of the sequences recited in SEQ ID NOS: 466-487, 510, 511 and 514-623; (c) reverse complements of the sequences recited in SEQ ID NOS: 466-487, 510, 511 and 514-623; (d) reverse sequences of the sequences recited in SEQ 466-487, 510, 511 and 514-623; (e) sequences having at least a 99% probability of being the same as a sequence selected from any of the sequences in (a)-(d), above, as measured by the computer algorithm BLASTP using the running parameters described above; (f) nucleotide sequences having at least 75% identity to any of the sequences in (a)-(d), above, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (g) nucleotide sequences having at least 90% identity to any of the sequences in (a)-(d), above, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (h) nucleotide sequences having at least 95% identity to any of the sequences in (a)-(d), above, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (g) open reading frames of SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623.
 - 2. An expression vector comprising an isolated polynucleotide of claim 1.
 - 3. A host cell transformed with an expression vector of claim 2.
- 4. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 488-509, 512, 513 and 624-725; (b) sequences having at least a 99% probability of being the same as a sequence of SEQ ID NOS: 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters described above; (c) sequences having

at least 75% identity to a sequence provided in SEQ ID NOS: 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 90% identity to a sequence provided in SEQ ID NOS: 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (e) sequences having at least 95% identity to a sequence provided in SEQ ID NOS: 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (f) sequences encoded by a sequence provided in SEQ ID NOS: 488-509, 512, 513 and 624-725.

- 5. An isolated polynucleotide encoding a polypeptide of claim 4.
- 6. An expression vector comprising an isolated polynucleotide of claim 5.
- 7. A host cell transformed with an expression vector of claim 6.
- 8. An isolated polypeptide comprising at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 196, 488-509, 512, 513 and 624-725; (b) sequences having at least a 99% probability of being the same as a sequence of SEQ ID NOS: 196, 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters described above; (c) sequences having at least 75% identity to a sequence provided in SEQ ID NOS: 196, 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above; (d) sequences having at least 90% identity to a sequence provided in SEQ ID NOS: 196, 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above; (e) sequences having at least 95% identity to a sequence provided in SEQ ID

NOS: 196, 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above; and (f) sequences encoded by a sequence provided in SEQ ID NOS: 466-487, 510, 511 and 514-623.

- A method for stimulating keratinocyte growth and motility in a patient, comprising administering to the patient a composition comprising a polypeptide of claim
- 10. The method of claim 9, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398; (b) sequences having at least about 50% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least about 75% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least about 90% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196.
- 11. A method for inhibiting the growth of cancer cells in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 12. The method of claim 11, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 342, 343, 397 and 398; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90%

identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196.

- 13. A method for modulating angiogenesis in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 14. The method of claim 13, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 342, 343, 397 and 398; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196..
- 15. A method for inhibiting angiogenesis and vascularization of tumors in a patient, comprising administering to a patient a composition comprising a polypeptide of claim 4.
- 16. The method of claim 15, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 342, 343, 397 and 398; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS:

187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196.

- 17. A method for modulating skin inflammation in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 18. The method of claim 17, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 338 and 347; and (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 338 and 347 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 338 and 347 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 338 and 347 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.
- 19. A method for stimulating the growth of epithelial cells in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 20. The method of claim 19, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 129 and 348; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 129 and 348 as measured by the computer algorithm BLASTP using the running parameters and identity

test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 129 and 348 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 129 and 348 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.

- 21. A method for inhibiting the binding of HIV-1 to leukocytes in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 22. The method of claim 21, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 340, 344, 345, 346 and 465; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.
- 23. A method for treating an inflammatory disease in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 24. The method of claim 23, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 340, 344, 345, 346 and 465; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90%

identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.

- 25. A method for treating cancer in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 26. The method of claim 25, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 340, 344, 345, 346 and 465; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.
- 27. A method for treating a neurological disease in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 28. The method of claim 27, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397

and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196.

SEQUENCE LISTING

<110> Watson, James D. Strachan, Lorna Sleeman, Matthew Onrust, Rene Murison, James G. Kumble, Krishanand D. <120> Compositions isolated from skin cells and methods for their use <130> 11000.1011c4U <160> 725 <170> FastSEO for Windows Version 3.0 <210> 1 <211> 696 <212> DNA <213> Rat <400> 1 aattcggcac gaggccgagg cgggcaggca ccagccagag cagctggcgg cagacagtcg gaccgagaca gttggaccga gacagtcgaa cggtctaaca gggcctggct tgcctacctg 120 gcagctgcac ceggtccttt teccagaget ggttetgtgg gtcaacatgg teccetgett cotcotgtot otgotgotac ttgtgaggco tgcgcctgtg gtggcctact ctgtgtccct 240 cccggcctcc ttcctggagg aagtggcggg cagtgggggaa gctgagggtt cttcagcctc 300 ttccccaagc ctgctgccgc cccggactcc agccttcagt cccacaccag ggaggaccca 360 gcccacaget ccggtcggcc ctgtgccacc caccaacete ctggatggga tcgtggactt 420 cttccgccag tatgtgatgc tcattgcggt ggtgggctcg ctgacctttc tcatcatgtt 480 catagtotgo goggoactoa toacgogoca gaagcacaag gocacageot actaccogto 540 ctctttcccc gaaaagaagt atgtggacca gagagaccgg gctggggggc cccatgcctt 600 cagcgaggtc cctgacaggg cacctgacag ccggcaggaa gagggcctgg acttcttcca 660 geageteeag getgacatte tggettgeta eteaga 696 <210> 2 <211> 475 <212> DNA <213> Rat <400> 2 cggtatcgat aagcttgata tcgaattcct gcaggtcgac actagtggat ccaaagaatt cggcacgaga aaataaccaa ccaaacaaac tttcctcttc ccgctagaaa aaacaaattc 120 tttaaggatg gagctgctct actggtgttt gctgtgcctc ctgttaccac tcacctccag 180 gacccagaag ctgcccacca gagatgagga actttttcag atgcagatcc gggataaggc 240 attgtttcac gattcatccg tgattccaga tggagctgaa atcagcagtt acctatttag agatacacct agaaggtatt tetteatggt tgaggaagat aacaccccac tgteagteac 360

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cagagacagt ccccgttttt aaacttcgac aattgacttt tatttccttt tctaattttt
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attattttt aaaacaacca ggatgattat cacatctact cccccatccg tccagaaaag
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ccccaaattg attecttcag ggtctggcct gcccaggctc tattccacat gtgcaggttc
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caacagetta accetattet etteccagte atetgetgea ggtatagetg teteatgece
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<212> DNA
      <213> mouse
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      <221> unsure
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gaacgcaaga gtccttatgt cgccatatgc tgtatagtga tggccttcag catcctcttc
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atacagtage tttggaaact accagcatgt gcttgctatc agactgtaaa caaggacttg
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cctccagaaa ataatgggaa gaatggttaa gccatttgtc tctgaacatg gaatgagata
                                                                      360
aacttcaaga tgctgttctc tatttttatg ctattggacc aatgagctga atgaataatt
                                                                       420
aagatgtaac agttcaatac acaggaatgt gattgtatcc atcaacctca gttctctcac
                                                                       480
tccagtatta cattctgcaa atgtcattct gttgtgtcag gactgctttt cataaggttc
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aataatgtct tcacagaatg gtacctctag cgactgtcct attnttattg agaaaaaaac
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                                                                      720
gattgctaac cagagtacct ctattcttgg caaattccgc agtttattac aggtgtttaa
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aagatacagc tgccacactg tgacgaagag caccttagaa agaaaagcag caagtgagcg
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                                                                       960
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tgtagtcttg tcttccaaat agaacgtcca tcgtagttac ccaaaggtgg tatttgtggt
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                                                                      1200
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qaattaaatc ctagctgaaa actatacata gcatttatta attaattact qggtttaact
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      <210> 35
      <211> 797
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catctggtgg ggaacacage geeggggete ggagaceatg gegggegetg eggtgaagta
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cgtggatcaa ctcatggagc tggccgggtt gagctgtgcc acggctattg ccaaggctta
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tecececacy tetatgteca agagtecece gaetgtettg gteatetgtg geeeeggaaa
                                                                       360
taacggaggg gatgggctgg tctgtgcgcg acacctcaaa ctttttggtt accagccaac
                                                                       420
tatetattae cecaaaagae etaacaagee eetetteaet gggetagtga eteagtgtea
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gaaaatggac atteetttee ttggtgaaat geecceagag gatgggatgt agagaaggga
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aaccctagcg gaatccaacc agacttactc atctcactga cggcacccaa gaagtctgca
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                                                                       660
actcacttta ctggccgata tcattacctt gggggtcgct ttgtaccacc tgctctagag
aagaagtacc agctgaacct gccatcttac cctgacacag agtgtgtcta ccgtctacag
                                                                       720
                                                                       780
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aaaaaaaaa aaactcg
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      <210> 36
      <211> 896
      <212> DNA
      <213> mouse
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```
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cccatcccag atttgcttag tttgtctccc aatgtgctgg actttaaaga cagggaatgg
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agaagcagat ggatgcttca gtttcagtca tttttggctc tatagtgatc tctgccttcc
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tgtacctgtc cttggctgga ccctgggcag taactgtcac tcagatgagg acgatcatca
                                                                     300
ttacaatgga ccaactgagg gatgccctca tattagacca attaaaagtt gctgtgagtt
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aaaccaggaa tgaccgcact tccacatcag aaatcaaaca aaatcaatgg ttgaagaaca
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tggttaggag cctggctagg tatctttgag agatggatgc agctggctac tcaggcaggt
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aagcaatgga ggtcagccac accctatcgt gatgcactcc ccatgttcag ggtaactgaa
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gaagtgggta aggccagctg aaggccagtc agggcaactt agatgtagcc tggcttctac
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ttccagcctc cggggacagg caaacacatt ttgggaagta agatgatgtc ccaattatta
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atgitactig gittaatgaa ggcccctca accccaacag ccctcctgc tcagggacac
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                                                                     120
cagcatcgtt cttatatgcg actaacagaa aaggaagatg aatcattacc aatagatata
                                                                     180
gttcttcaga cacttctggc ctttgcagtt acctgttatg gcatagttca tatcgcaggg
                                                                     240
gagttcaaag acatggatgc cacttcagaa ttaaagaata agacatttga taccttaagg
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aatcacccat ctttttatgt gtttaaccat cgtggtcgag tgctgttccg gccttcagat
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gcaacaaatt cttcaaacct agatgcattg tcctctaata catcgttgaa gttacgaaag
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                                                                     501
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     <211> 766
     <212> DNA
     <213> mouse
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ggcgtactgg agcgagccga gcagagcaga gagaggcgtg cttgaaaccg agaaccaagc
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cgggeggeat ecceeggeeg ecgeaegeae aggeeggege ceteettgee tecetgetee
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ccaccgcgcc cctccggcca gcatgaggct cctggcggcc gcgctgctcc tgctgctcct
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ggcgctgtgc gcctcgcgcg tggacgggtc caagtgtaag tgttcccgga aggggcccaa
                                                                     300
gatccgctac agcgacgtga agaagctgga aatgaagcca aagtacccac actgcgagga
                                                                     3.60
gaagatggtt atcgtcacca ccaaagagca tgtccaaggt accggggcca ggagcactgc
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ctgcacccta agetgcagag caccaaacgc ttcatcaagt ggtacaatgc ctggaacgag
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aagcgcaggg tctacgaaga atagggtgga cgatcatgga aagaaaaact ccaggccagt
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600
ataagacaaa ttatatattg ctatgaagct cttcttacca gggtcagttt ttacatttta
                                                                     660
                                                                     720
tagetgtgtg tgaaaggett ceagatgtga gateeagete geetgegeae cagaetteat
tacaagtggc tttttgctgg geggttggeg ggggggggg ggacet
                                                                     766
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     <211> 480
     <212> DNA
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<213> mouse

```
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cgcctggcct ggcattatga atgcagtggg gtcagtgtgt ggtggatgtg tgtactgggt
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aatcattctc acatgcttcc atgtttgttt ctgagaggtg ggggctcaaa tgtatagaaa
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gtaggcccca gtccataagg aggtgtgaac acacccctt actgcttatc acccattga
                                                                   300
caggaacgcc caggagggga gggggagggg aagaggtgag ttctgcacag tcggacattt
                                                                   360
ctgttgcttt tgcatgttta atatagacgt tcctgtcgat ccttgggaga tcatggcctt
                                                                   420
cagatatgca cacgacettt gaattgtgcc tactaattat agcaggggac ttgggtaccc
                                                                   480
     <210> 40
      <211> 962
     <212> DNA
      <213> mouse
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cattcatctc teteteatte ecctgetetg catectgatg agaaactgtt tggettttaa
                                                                   120
aaatgatgcc acagaaatcc tttattcaca tgtggttaaa cctgtcccgg cacaccccag
                                                                   180
cagcaacagc accetgaate aagceaggaa tggaggeagg cattteagta geactggaet
                                                                   240
ggatcgaaac agtcgagttc aagtgggctg cagggaactg cggtccacca aatacatttc
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caagaggtac acceptcage acaacgagte cagecacaac tttgaaageg tgtegceage
                                                                   600
caagecegee cageaceaea gagageggaa gagageeage aaateeagea ageaeagtet
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ctctctcgag cctgccattg ctctttcctc acttgaaagt atatgctttc tgctttgatc
                                                                   780
aagcccagca ggctgtcctt ctctgggact agcttttcct ttgcaagtgt ctcaagatgt
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aatgagtggt ttgcagtgaa agccaggcat cctgtagttt ccatcccctc ccccatccca
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960
                                                                   962
aa
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     <211> 794
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ggtggggaac acagegeegg ggeteggaga ccatggeggg egetgeggtg aagtaettaa
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gaggggatgg gctggtctgt gcgcgacacc tcaaactttt tggttaccag ccaactatct
                                                                   420
attaccecaa aagacetaac aagceeetet teaetggget agtgaeteag tgteagaaaa
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tggacattcc tttccttggt gaaatgcccc cagaggatgg gatgtagaga agggaaaccc
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ctttactggc cgatatcatt accttggggg tcgctttgta ccacctgctc tagagaagaa
                                                                   660
gtaccagetg aacctgccat ettaccetga cacagagtgt gtetaccgte tacagtaagg
                                                                   720
gaggtgggta ggcaggattc tcaataaaga cttggtactt tctgtcttga aaaaaaaaa
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aaaaaaact cgag
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<210> 42
      <211> 1152
      <212> DNA
      <213> mouse
      <400> 42
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caggetggge cacaggaage tgetgactgg ceaettgaca eceteceet aaagetaatg
                                                                     120
totgtgacta tagggaggtt agcacttttt ctaattggaa ttcttctctg toctgtggcc
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ccatccctca cccgctcttg gcctggacca gatacatgca gcctctttct ccagcacagc
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ctttccctga gcctgaggtt agggcagagt ttagagggtg ggctaagtgt atgttttcat
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gtatgcattc atgcctgtga gtgtgtggct tgctgtcgtg tcctctggga tcccaagcca
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cgcgggtctt ccctctgtag atgggtcctg ggttctatca cctgcttatt tatgtacgag
                                                                     420
gttgggggt ggacccaggg tgggttgatt gtctctttgt aaggaagtat gtgtcggggg
                                                                     480
tgacacgagg ctaagcccga gaaaccccgg gagacagcac tgcataagaa actggtttcc
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600
aaacaaaaca aaaataactc tgaagggcgg gaggataccc aagcctgatg cctgagagga
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accetgtete etggeattgg geteeggete taceteecea ageagggega ggeecegeet
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teteagecta geaceacetg teecegagte tteteagett geecateatt eteggegee
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gcetgcccag cc
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ccaggtcctc tggagaaata accagtgctc ttaaccacta agccatctca acagccccaa
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ctaatataga ttatttatga attcaggtgg cttaatggta tatgcatgaa ttagtagtaa
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aacaagaact agggccagca agtggcttaa gggtgcctgc taaccatctc agccacctga
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gttcagtctc caggaaccac acagtg
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      <212> DNA
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                                                                     120
acacagagac agatgccgtg agctccagaa gtaatggacg gcccccact gctggcgctg
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tececaaate tgegaaatac ategeteagg tgetgeagga eteagagggg gaeggggaeg
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gagatggggc tcctgggagc tcaggcgatg agcccccatc gtcctcctcc caagacgagg
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agttgctgat gcctcctgat ggcctcacgg acacagactt ccagtcatgc gaggacagcc
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                                                                     391
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gcccacaget ccggtcggcc ctgtgccacc caccaacetc ctggatggga tcgtggactt
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                                                                       360
                                                                       420
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cagcgaggtc cctgacaggg cacctgacag ccggcaggaa gagggcctgg acttcttcca
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      <213> mouse
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ccccag
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      <211> 439
      <212> DNA ·
      <213> mouse
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catchttctc thtctcttt totgtttctt gttccccttt ccccttttcc tggtgagaaa
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gcacatatta ctgagccatt gcaagcaatg ggaggggtcc acaatgacac acacacaca
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tgtattttgg ccaaacttgg aaaataggtt tccttcttcg ttttgcttcc agccttttat
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ttqcaaqtqa tcttccatqc aqtatgaaac atgcagacag cactggagtg tggcaagagt
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gagettgeec cacaagtete teggggatgt tgtactettg tgtgtgttta cagtateatg
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gctgttacat ctactggtc
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      <211> 159
      <212> DNA
      <213> mouse
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      <221> unsure
      <222> (3)...(3)
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```

```
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      <213> Rat
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                                                                       300
                                                                       360
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gaggggtga getecegete egeteggatt tetteggace tteteaggaa catagtgeet
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      <211> 337
      <212> DNA
      <213> Rat
      <220>
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ctcagaacat atacaacctg tacgagcaag tcagctacaa ctgtttcatc gccgcgggcc
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      <211> 371
      <212> DNA
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21

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PCT/NZ01/00099 WO 01/90357

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gtgcaacgac agcagtgtct actataactt gacatcccaa agccagtcgg tcttccagac
                                                                       420
aaactggaca gttcctactt ccgaggatgt gactaaagtc aacctgcagg tcctcatcgt
                                                                       480
cgtcaatcgc acagcctcaa agtcatccgt gaaaatggaa caagtacaac cctcagcctc
aaccectatt cetgagagtt etgagaccag ecagaccata aacacgacte caactgtgaa
                                                                       540
cacagccaag actacagcca aggacacagc caacaccaca geegtgacca cagccaatac
                                                                       600a
                                                                       660
cacagecaat accacagecg tgaccacage caagaccaca gecaaaagec tggccateeg
cactetegge agececetgg caggtgeect ceatateetg ettgttttte teattagtaa
                                                                       720
actoctotty taaagaaaac tggggaagca gatotocaac ctocaggtoa tootoocgag
                                                                       780
                                                                       840
ctcatttcag gccagtgctt aaacataccc gaatgaaggt tttatgtcct cagtccgcag
                                                                       900
ctccaccacc ttggaccaca gacctgcaac actagtgcac ttgagggata caaatgcttg
cotogatett teagggeaca aatteegett ettgtaaata ettagteeat eeateetgeg
                                                                       960
tgtaacctga agttctgact ctcagtttaa cctgttgaca gccaatctga acttgtgttt
                                                                      1020
cttgccaaag gtattcccat gagcctcctg ggtgtggggg tggggaggga atgatccttc
                                                                      1080
tttactttca aactgatttc agatttctgg ccaaacctac tcaggttgca aaggacttat
                                                                      1140
                                                                      1200
gtgacttatg tgactgtagg aaaaagagaa atgagtgatc atcctgtggc tactagcaga
tttccactgt gcccagacca gtcggtaggt tttgaaggaa gtatatgaaa actgtgcctc
                                                                      1260
                                                                      1320
agaagccaat gacaggacac atgacttttt ttttctaagt caaataaaca atatattgaa
                                                                      1335
caaggaaaaa aaaaa
```

```
<210> 77
      <211> 440
      <212> DNA
      <213> mouse
      <220>
      <221> misc_feature
      <222> (1)...(440)
      <223> n = A,T,C or_G
cactagggnc tecaaagaat teageacgag gagaageett geecaeteaa atacetggge
                                                                    60
catcagctgc accggctcca ctcccatctg ctccaggccc tgaagagaag ccaacacttt
                                                                   120
traggeret caaceterar atragaarag gragageetg tggtgtrage tgttgatera
                                                                   180
aaggcaaccc ttggtggggt tggggttgta aagtagtgat gctaatttct aagcaacaag
                                                                   240
ctctgagctg cagcccccag gccctccagg gcagtccagg gcagtgccag ggttcagggt
                                                                   300
agttctaggg gtctagtatc tggatcaaca agtcccagag ttgggcccag tggctgctga
                                                                   360
                                                                   420
cttgttcaat gaccaagaat atacgaccta accttttta tttggttggg caaccacagc
                                                                   440
tccgagtaag tcatcaaggc
       <210> 78
      <211> 204
       <212> DNA
       <213> mouse
      <400> 78
 ctccataaaa ttcctcaaaa tctgttcccc cagcagattt cctgtgccat cttgggctcc
                                                                    120
 cttcctattc tttcccgtct ttagggcctc ctcacagtgt tgttttctaa caacgcaggc
 204
 cctctgtgtc ctcttcatcc caat
       <210> 79
       <211> 300
       <212> DNA
       <213> mouse
     · <220>
      <
       <400> 79
tatttatgac ttgggttaag ggagtttgct gtgcaatcat gaagaccaga gttcagatcc
                                                                   ·60
cagcacccat atagcaagag agcatacaag aagcacctgt gactgcactc tgaagaatcc
                                                                   120
aacaccttet tetggeetee atggeacaca gaacccccca acacatgete atccactete
                                                                   180.
                                                                   240
aaagagacat acataaaaat aaatatttag gtcctgggtc cctcagagac tagtcttcac
aggtcctaaa tacaaacgna gcggaccgca aagggtgagg gagtggncct gaagaagcta
                                                                   300
       <210> 80
       <211> 214
       <212> DNA
       <213> mouse
 cccagaccct gtgtcagcta tcccagcaga aaaagaagat gcggaccctc tcagcaagtc
                                                                     60
 aggtgaggaa acccaggaag cagggtcatg accccgcaga ggtcggggct cctggtgcag
                                                                    120
 aggatcagat cttgtgtgac ttctgtcttg gggccagcag agtaagggca gtgaaatcct
                                                                    180
 gtctgacctg catggtgaaa tactgtaagg agca
```

```
<210> 81
      <211> 152
      <212> DNA
      <213> mouse
      <220>
      <400> 81
ccccttaact aacccaggac cttccactaa gtggaaggct ccaccatcca cagaggggc
cagicattit taagcacacg gacctitigt gagacagtcg tgatcttaac tgtggtgtca
                                                                      120
ctgatggagc tgaacggtat cccctaaaag ta
                                                                      152
      <210> 82
      <211> 181
      <212> DNA
      <213> mouse
      <220>
     <400> 82
teteagtgat gatgagaage teeggaggag geaggagaaa geagggeece geeceteect
gggtctccac ccacccacgc ccgctaaggt cacctgttct cccatggaga tgatgaagaa
                                                                      120
getcataget ggacaaggee eggaacetea geceagtaac egacetaett eeegeetggg
                                                                      180
                                                                      181
      <210> 83
      <211> 332
      <212> DNA
      <213> mouse
      <220> ·
     <400> 83
tatagagatg gtgatgtaat gggccagggt gtaagettca acctggggga ttttgctggt
                                                                       60
tttgttgttt ccctgtgtag ccctaacaag cctgtgtaga ccaggctggc tttaactttg
                                                                      120
cagatgacat tcacgtctac ttctctctgt gttggggtta tgggtctgca cacctgccca
                                                                      180
ggcctaggct gggggatttt gaagtatctt agattatgga gtagacccag agtttgcaag
                                                                      240 -
tatctgcttt aaagtgacac ataaacatag cctcctgacc atcttccaca gtgggaccct
                                                                      300
gatctggcct ctccctggaa gaagagagaa ag
                                                                      332
      <210> 84
     <211> 213
      <212> DNA
      <213> mouse
     <400> 84
gcaggcagat aacaatgatt actggacaga gtgcttcaac gcattggaac aggggaggca
                                                                       60
atatgtggat aatcccacag gcgggaaagt ggacgaggct ctggtgagaa gtgccaccgt
                                                                      120
acattgttgg ccgcacagca acgtgctgga cacaagcatg ctctcatccc cagatgtggt
                                                                      180
gcgcatgctg ctgtccctgc agcccttcct gca
                                                                      213
      <210> 85
```

<211> 273

```
<212> DNA
       <213> mouse
       <220>
       <221> misc_feature
       <222> (1)...(273)
       <223> n = A,T,C or G
       <400> 85
ceggetetet eteteeteet teecegeete ttetgeetee eetgeetgga aetetgatga
                                                                       60
ggagggacca ggtggtcagg caccccagtc tgatcaggac tcctgtggcc tccagagttt
                                                                      120
cantececeg tecatectga agegggetee tegggagegt ceaggteang tggeetttaa
                                                                      180
eggeateane gtetactatt teccaeggtg ceaaggatte accagtgtge ceaageegtg
                                                                      240
gtggctgtac cctgggnatg gcttctcggc aca
                                                                      273
       <210> 86
       <211> 218
       <212> DNA
       <213> mouse
       <400> 86
 ctcagccgcc tgctctgggg gctggagggt ctcccactta actgtgtctg ccgttcaggg
 ggctcaccca gtgctgcgct acacagaggt tttccctcca gctccagtcc gtcctgccta
                                                                       120
 ctecttetat aacegeetee aagagetgge etcactgttg eeceggeegg ataageeetg
                                                                       180
 cccagcctat gtggagccta tgactgtggt ttgtcacc
                                                                       218
       <210> 87
       <211> 335
       <212> DNA
       <213> mouse
       <400> 87
 gaggtggggt gggtgcatag cctgcctgca attgctgccg ctgggcttaa cgtgttgtga
                                                                        60
 gctggccggt ttcctacaca gcagcacctg ccatggagcc tggccacaag gccactcaga
                                                                       120
 gctgggtgga cagagtgtga ccagaaactc cctgtgggtt ctgataaagg attctcccat
                                                                       180
 aggcaaggtt cagagaacct gggcctcctg ttctcaggga ggcctgtcta tccccagcct
                                                                       240
 ctgagctgtt tcgtcctagt tggtgagtta agtggcatag ccctcttgag gcctctgatg
                                                                       300
 tggaaggggc acagaattgc aattattctt gcatg
                                                                       335
       <210> 88
       <211> 410
       <212> DNA
       <213> mouse
      <400> 88
 aaaccccgcc aggaaacaaa taccggtgta tcggctttac tgaatgcatt tattcccaaa
                                                                        60
 gggaaactga aaagcaacct agggacactg taagcagaaa gctgaggctt ttaaaaaaccc
                                                                       120
 accttggcaa tgtaacttgg gaggttccca cacacccagg gctgtgcatc gtgaaattct
                                                                       180
 gtctcctgag acgctgagaa acccttcctt gcagctataa tgggcctggc cgcccagtgt
                                                                       240
 ggagctgtag cttcccacga cgtagccctc aggaacttca ggagggatgc cacagtctat
                                                                       300
 ttctgaaaac aaaaccgtgt caacttcttt actttacaaa tgcaagtttt cagaatccac
                                                                       360
 catctctctg cacccatacc ccatgcctca caccccagac cctgtgttag
       <210> 89
       <211> 279
       <212> DNA
       <213> mouse
```

<220>

```
<400> 89
gtgcagagag tggattgtca gtggactgct cagttacaaa tgggacatct aacacacaca
                                                                  60
cacacacaca cacacacaca cacacacaca Caccccaagg cttagagacc attgcagaag
                                                                 120
agaagagttt atgggaaatc ttggagaaaa cattggatgg tttgagagaa tggttaggag
                                                                 180
240
gacagggtgg agggcattgt ccgacagaac cattgctgt
                                                                 279
     <210> 90
     <211> 398
     <212> DNA
     <213> mouse
     <400> 90
ccaccaaccc agaaatttga caaaggggtt gaatgttgga ctttgcgtcc ttccccggca
                                                                  60
gtggatgtac tgttttgagc cctgtgtgga acttctgaac ttcgtgctgt aactttcaga
                                                                 120
actettagac atgggtgtgc tcactgaact ctagggtctg tgtgctagat gctgccaacg
                                                                 180
ctgtattcag gacctgaagt gagtacccgt gtggatccag accaatccag tgtgagacta
                                                                 240
ctgaagaaca tctgttgcca gaacggccac accaaacaga tggagtgccc cagcacttag
                                                                 300
cttcttaaat aacatcggaa ccattcagcc agcgagtctg tgtttgcttt ttgttaaatt
                                                                 360
gtccgccgaa tctaaattcc tccaaaaggc ttgtgacc
                                                                 398
     <210> 91
     <211> 279
     <212> DNA
     <213> mouse
     <400> 91
gttgttactt cagttgctct cggcgggaat tcttaaactg catcctgagt gagggagctt
                                                                  60
tggcgagaaa gcaagaccca gtggtagaca gattagcatt actgtacagc ttctttgggt
                                                                 120
                                                                 180
gttcgaggaa gcccggctgg accatagtgg ccacggcggt gaggtaggcg tggacagggc
tqaccagtcc aagttaagga cgttcgggtc catgttaacc ctgccttgta cgtccagcat
                                                                 240
                                                                 279
cgtaagaaaa aacacttgag aacccgaaga ggagatgga
     <210> 92
     <211> 401
     <212> DNA
     <213> mouse .
     <400> 92
aaaaagtttt accaaaacct tttattgact tttataaatt agatagtatt tcaaagttta
                                                                  60
120
cacgetetge aatgaateat gtggcaccga gtetacgeca aggeeeccga gaaaetttat
                                                                 180
tccatagatg ggcagatggt tcccaaagtt acactacaga actacaaatc gactcttaaa
                                                                 240
                                                                 300
attaaaacgg gactttacaa gcattctaga agactcaaac ttgaagcaat ttttggaaaa
taaatgtaca gagaaaagat cttgaagcta ctgaacagag aaccctcatt aaccgagcaa
                                                                 360
                                                                  401
atacatecta tggagettee gaggagtaea cagacagaee g
     <210> 93
      <211> 339
      <212> DNA
     <213> mouse
     <400> 93
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ccactgacct tcccagaagg tgacag ccagcagtgc ctcggtaccc agaaga atgagaagtc accacagtga tctcac catgatgcag cctggccttt cctaga cgtgtcatca agaaccctat ggattt	acggg ctgtctccc cattt tgcgagatta agcct gtgaaccctc cttcc accatgcgag	ccaaaagacg tcctgatgga gcttggtgag	gcgacattcg gatggagtcc tggataccga	120 180 240 300 339
<pre></pre>	egat getetgetg		٠.	333
<pre><400> 94 ggggtgtggg caacttggat aacctc <210> 95 <211> 186 <212> DNA <213> mouse</pre>	aget gettecatet	ggctgacatc	tttgg	55
<pre><400> 95 ggactctggc ttcctggggc tgcggg gcggggcccc agaaacaaga agcgcgagaggcgac cagttcctgg aagacgggaga</pre>	ggctg gaggaggctc	gccgaggagc	cgctggggtt	60 120 180 186
<210> 96 <211> 244 <212> DNA <213> mouse <400> 96				
ggtgaccaaa acccettetg cccce cccteteccc aaggccatgg attat aagagggcat gaggcacacc ctgat ctggcccacc tcacgcccc aggcc	gaagc ccctctgtaa cactg tctcaggcct	gatggtgagc ttgtgggcac	caggggccct tgactcgacc	60 120 180 240 244
<210> 97 <211> 116 <212> DNA <213> mouse			·	. cs,
<220> <pre> <221> unsure <222> (11)(11)</pre>		.,		•
<221> unsure <222> (13)(13) <221> unsure <222> (41)(41)				
<400> 97 acccggtctg ngnactgccc gcctt atctaggact cctgccaccc tgact	ctggg getteetta getga ettacageta	naggatacag tgaggteceg	tettttaccc gettet	60 116

```
<210> 98
       <211> 307
       <212> DNA
       <213> mouse
       <400> 98
ccccgggcca tctgtcgcca taccgggccc gtgcaagctt ttgcaggttt tagaagatgg
                                                                         60
cgaattcatg acacetgtga tecaggacaa cecetcagge tggggteeet gtgeegttee
                                                                        120
 tgagcaattt cgggatatgc cctaccagcc attcagcaaa ggagatcggc tgggaaaggt
                                                                        180
 tgcagactgg acaggggcca cataccagga caagaggtac acaaacaagt attcctctca
                                                                        240
gttcggtggg gggagtcagt atgcatattt ccatgaggag gatgagacaa gctttccagc
                                                                        300
                                                                        307
 tgggtgg
       <210> 99
      <211> 360
       <212> DNA
       <213> mouse
       <220>
       <221> misc_feature
       <222> (1) ... (360)
       <223> n = A, T, C \text{ or } G
       <400> 99
cettggtgca ccagetccag cetcaggact tecteeteet ggeeetgaca geccagetet
                                                                       120
tgtcccagca gaatccagtg acaggaagga gtttctgagg caggggagga ggcttctcca.
tgggaaccag acagcettge tteactgtat aagtgeeetg ateacacgea gaatgaagtg
                                                                       180
ccaggttgct cagaagcaca aagggtgtgg ctactggccc taaccatgga ctacgtggtt
                                                                       240
                                                                       300
ctaaccaaag actctagaac tctggggtgg gggagaaaca atgtgttctg tgctccagaa
ccttnggctt cctggcccat atggatgggc ttggcaagga acctacctct tctctaaggt
                                                                       360
       <210> 100
       <211> 257
       <212> DNA
       <213> mouse
       <400> 100
                                                                          60
 tgecgegetg agagggggg eegeaceace agegeeacea ceaceacege egeegeege
 gggtggggtg ggagggggg gagccaccgc taccgccgcc gcctcccggg tgggcgccct
                                                                         120
                                                                         180
 tctccttaga cgccggcgac ccaggacgag ggcttcatca ctgtaaatgg ttgcaagccg
 acaaagetge aceteetgaa aaagaeggae ageeeatege gtgagetgta gaaatttgtg
                                                                         240
                                                                        25%
 gacgcatttc tatcggt
       <210> 101
       <211> 203
       <212> DNA
       <213> mouse
       <400> 101
 ccaaagtgcc.cattgtgatt caagacgata gccttcccac ggggccccct ccacagatcc
                                                                          60
 gcatcctcaa gaggcccacc agcaacggtg tggtcagcag ccccaactcc accagcaggc
                                                                         120
                                                                         180
 cagcccttcc tgtcaagtcc ctagcacagc gggaggCaga gtatgcagag gctcggagac
                                                                         203
 ggatectagg cagtgecage cet
       <210> 102
       <211> 300
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<212> DNA
     <213> mouse
     <400> 102
agtacagaga ceteggetge agettaaace teggacagtg geaacgeece teaatcaagt
                                                                        60
                                                                       120
agccaaccc aactcagcca tctttggggg agccaggccc agagaggaag tggttcagaa
ggagcaagaa tgagcttagg ttgggaggga atggggcgtg ggggagctgg agcaagacca
                                                                       180
eggeetggtg geageeggte geeetacagg ecceatteee geetggeact gteeteetta
                                                                       240
cageggaaac acagagettg tgagtgcatg teagetgtta acaagtggtt tetagtacat
                                                                       300
      <210> 103
      <211> 370
      <212> DNA
      <213> mouse
      <220>
     <400> 103
                                                                        60
cagcaactgt ttcaggagct gcacggtgta cgcctgctga ctgatgcgct ggaactaaca
ctgggcgtgg cccccaaaga aaaccctccg gtgatgcttc cagcccaaga gacggagagg
                                                                       120
gccatggaga tcctcaaagt gctctttaat atcacctttg actctgtcaa gagggaagtt
                                                                       180
gatgaggaag atgctgccct ttaccggtac ctggggactc ttctgcggca ctgcgtgatg
                                                                       240
                                                                       300
gttgaagctg ctggggaccg cacagaggag ttccacggcc acacggtgaa tctcctgggg
aacttgcccc tcaagtgttt ggatgtgctt ctggccctgg agctccacga aggatcctta
                                                                       360
                                                                       370
gagtcaatgg
      <210> 104
      <211> 423
      <212> DNA
      <213> mouse
      <400> 104
tttcccagcc tggtggagca gccgactggc gagtgtgcca actgtcccgt gcttcccagc
                                                                        60
tectacettg cetgtettet eteteetggg aagatgttee tggtgggget gaegggagge
                                                                       120
ategeeteag geaagagete egteateeag gtatteeaac agetgggetg tgetgtaate
                                                                       180
                                                                       240
gacgtggacg tcattgcgcg gcacgttgtc cagccagggt atcctgccca ccggcgtata
                                                                       300
gtagaggeet tiggeactga agtetigetg gagaatggeg acategaceg caaggieete
                                                                       360
qqaqacetqa tetteaacea qeetqaceqt eggeagetge teaacteeat tacceacect
                                                                       420
gagateegea aggaaatgat gaaggagace tteaagtaet teteegaggt accgataegt
gat
                                                                       423
      <210> 105
      <211> 117
      <212> DNA
      <213> mouse
                                                                        60
agettggtge tgttcatatt taaactgata aagactette ataggagetg agggtageaa
gcccgcgtcg gtgactgggg tctcacacag gttcagcact tggagcatag tgaggtg
                                                                       117
      <210> 106
      <211> 133
      <212> DNA
      <213> mouse
      <400> 106
```

60

```
ttttttttt aaaataccac catttccaat cccaaaagaa catggcactt gtttgtttct
teceettete atteatteea gaettteaag tgttttette aataetgagg ettteteetg
                                                                       120
cagetetggt etg
                                                                       133
     <210> 107 <211> 217
      <212> DNA
      <213> mouse
     <220>
     <221> unsure
     <222> (1)...(1)
     <221> unsure
     <222> (11)...(11)
      <221> unsure
      <222> (18)...(23)
      <221> unsure
     <222> (34)...(34)
     <221> unsure
     <222> (37)...(38)
     <221> unsure
     <222> (40)...(42)
      <221> unsure
     <222> (50)...(52)
      <221> unsure
      <222> (55)...(58)
      <221> unsure
     <222> (152)...(152)
      <221> unsure
     <222> (155)...(155)
     <221> unsure
      <222> (165)...(165)
     <400> 107
ntttttttg ngcgcacnnn nnngnnnncg cccnggnngn nnagcctacn nncannnngt
                                                                       60
tttcttctcc aggctgaaga cctgaacgtc aagttggaag gggagccttc catgcggaaa
                                                                       120
ccaaagcagc ggccgcggcc ggagcccctc ancancccca ccaangcggg cactttcatc
                                                                       180
gcccctcctg tctactccaa catcacccct taccaga,
                                                                       217
     <210> 108
      <211> 346
      <212> DNA
     <213> mouse
     <220>
     <400> 108
```

```
gggcatagaa qgcatctcga aaaqaatact tatttgaatt gaaggaagat gaagagqcct
gcaggaaggc tcagaagaca ggagtgtttt acctctttca tgacctggat cctttgctcc
                                                                       120
aggegteagg acategatac etggtgeece ggettageeg ageagagttg gaagggetge
                                                                       180
tgggtaagtt cggacaggat tcgcaaagaa ttgaagattc ggtgctggtt gggtgctccg
                                                                       240
agcagcagga agcatggttt gctttggatc taggtctgaa gagtgcctcc tccagccgtg
                                                                       300
gacaagtatc gctgctccag cagcttgact gctgtaaaga ggatct
                                                                       346
       <210> 109
       <211> 242
       <212> DNA
       <213> mouse
       <400> 109
ccacattgtc cacaactgga aggcacgatg gttcatcctt cggcagaaca cgctcctgta
                                                                        60
ttacaagcta gagggtggcc ggcgagtaac cccgcccaag gggaggattg tccttgatgg
                                                                       120
 ctgcaccatc acctgccct gcctggagta tgaaaaccgg ccgctcctca ttaaactgaa
                                                                       180
                                                                       240
gacccgaact tccactgagt acttcctgga agcctgttct cgagaggaga gagactcctg
                                                                       242
       <210> 110
       <211> 310
       <212> DNA
       <213> mouse
       <220>
       <221> misc_feature
       <222> (1)...(310)
       <223> n = A,T,C or G
       <400> 110
                                                                       60
cccggccggg aatccaggtg gtagctggtg gagtcgcctc cggagagtga cgcgcagact
eggeteece geggeeegee eteetgeegg cetegeegeg gteteecttg eteectgaga
                                                                      120
                                                                      180
tegetgageg etgageageg geeegggaga ggaggeettg ggegaegggg egeggagagg
                                                                      240
gagggcggc gggcantggg ggcgccgcgg atctctatat ggcgacgggt ctgtcgggtc
tggctgtccg gctgtcgcgc tcggccggnc ggccggttcc tatgggggtct tctgcaaagg
                                                                      300
                                                                      310
ggttgacccg
       <210> 111
       <211> 228
       <212> DNA
       <213> mouse
       <400> 111
ttctttttta acatttggtg gtttttttct ttactctttt tttcttttcc ttcttttct
                                                                        60
 gccctcaacc ccccaactcc tttggtatga agtactttta acatttatat ttcattgtta
                                                                       120
 cactttaaat tttgtaagga aaactctgat atttcattcc tcctgaacca ctaatgttag
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 aatttatttc taagaatcag tcaacatgta tactcttaat agtgaatt
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 ctggtggcat ggactatggt atggttggtg gcaaggaggc tgggaccgag tctcgcttca
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 aacagtggac ctcaatgatg gaagggctgc catctgtggc cacacaagaa gccaccatgc
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				aggiticacca tcctgctggt		240 292
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tgcatgtgcg	tgaacagccg ctcttggtct gttttattcc	ttccacttat	tgcctcgttc	gtgtgtgatt gtaagaaacc aatgtacaga	aaccataagg	60 120 180 197
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aaaacatttc aacataggtg gtcatataca	aaaacagcca	aacacataat atatatactt	gtacaatctg	aaaaaaacaa gtgttccagg tatattatga	acaaacatct	60 120 180 205
<211: <212:	> 116 > 202 > DNA > mouse			·	ė	
<220	·			٠.		·
cctccctcat tgcacacaca cacacacaca	cacacacaca	cacacacaca atagttactt	cacgaacaca	tttctcattc cgcacacaca ccattcctag	cacacacacg	60 120 180 202
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cgcttctgct gtgtgaagga gcgcaagccc tggagtgcta cagctgcgtg cagaaggcgg
                                                                    120
acgatggatg cgctccgcac aggatgaaga cagtcaaatg tggtcccggg gtggacgtct
                                                                    180
gtaccgagge cgtgggageg gtagagacca tecacgggca attetetgtg geggtgeggg
                                                                    240
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     <211> 527
      <212> DNA
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gtgactgtaa cacctccaat cacagcccag caaggtaact ggacagttaa caaaacagaa
                                                                    180
geteacaaca tagaaggace catageettg aagtteteac acetttgeet ggaagateat
                                                                    240
aacagttact gcatcaacgg tgcttgtgca ttccaccatg agctagagaa agccatctgc
                                                                    300
aggtgtttta ctggttatac tggagaaagg tgtgagcact tgactttaac ttcatatgct
                                                                    360
gtggattctt atgaaaaata cattgcaatt gggattggtg ttggattact attaagtggt
                                                                    420
tttcttgtta ttttttactg ctatataaga aagaggtgtc taaaattgaa atcgccttac
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aatgtctgtt ctggagaaag acgaccactg tgaggccttt gtgaaga
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gegetggtee gggtgeeete ageeegggee gggcagatge egegeeeege agagegeggg
                                                                    120
ccccagtac ggctcttcac cgaggaggag ctggcccgct acagcggcga ggaggaggat
                                                                    180
caacccatct acttggcagt gaagggagtg gtgttcgatg tcacctctgg gaaggagttt
                                                                    240
                                                                    300
tatggacgtg gagcccccta caacgccttg gccgggaagg actcgagcag aggtgtggcc
aagatgtege tggateetge agaceteact catgacattt etggteteac tgecaaggag
                                                                    360
ctggaagccc tcgatgacat cttcagcaag gtgtacaaag ccaaataccc cattgttggc
                                                                    420
                                                                    480
tacacggccc gcaggatcct caacgaggat ggcagcccca acctggactt caagcctgaa
gaccagccc attttgacat aaaggacgag ttctaatgtc tagctgagaa gctggttcta
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Pro Val Val Ala Tyr Ser Val Ser Leu Pro Ala Ser Phe Leu Glu Glu
           20
                               25
                                                  30
Val Ala Gly Ser Gly Glu Ala Glu Gly Ser Ser Ala Ser Ser Pro Ser
                         40
                                            . 45
       35
Leu Leu Pro Pro Arg Thr Pro Ala Phe Ser Pro Thr Pro Gly Arg Thr
                                           60
    50
                       55
Gln Pro Thr Ala Pro Val Gly Pro Val Pro Pro Thr Asn Leu Leu Asp
65
                                ,
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Gly Ile Val Asp Phe Phe Arg Gln Tyr Val Met Leu Ile Ala Val Val
                               90
             85
Gly Ser Leu Thr Phe Leu Ile Met Phe Ile Val Cys Ala Ala Leu Ile
                  105
         100
                                           110
Thr Arg Gln Lys His Lys Ala Thr Ala Tyr Tyr Pro Ser Ser Phe Pro
                       120
      115
                                         125
Glu Lys Lys Tyr Val Asp Gln Arg Asp Arg Ala Gly Gly Pro His Ala
                                   140
           135
 130
Phe Ser Glu Val Pro Asp Arg Ala Pro Asp Ser Arg Gln Glu Glu Gly
              150
                         155
Leu Asp Phe Phe Gln Gln Leu Gln Ala Asp Ile Leu Ala Cys Tyr Ser
                              170
              165
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Met Glu Leu Leu Tyr Trp Cys Leu Leu Cys Leu Leu Leu Pro Leu Thr
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                         10
Ser Arg Thr Gln Lys Leu Pro Thr Arg Asp Glu Glu Leu Phe Gln Met
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                           25
                                             3.0
Gln Ile Arg Asp Lys Ala Leu Phe His Asp Ser Ser Val Ile Pro Asp
     35
                     40
                                       45
Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr Pro Arg Arg Tyr 50 55 60
                  55
Phe Phe Met Val Glu Glu Asp Asn Thr Pro Leu Ser Val Thr Val Thr
                         75
65 70
Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu Ser Leu Gln Glu Leu Pro
          . 85
                            . 90 '
                                                95 -
Glu Glu Ser Ser Ala Asp Gly Ser Gly Asp Pro Glu Pro Leu Asp Gln
         100
                           105
Gln Lys Gln Gln
       115
     <210> 122
     <211> 64
     <212> PRT
     <213> Human
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Met Asn Leu Leu Ile Gly Ser Ile Ile Leu Ser Ser Phe Leu Val Leu
1 5
                              10
Ser Asp Gly Asp Thr Thr Ala Ser Pro Ser Ser Met Ser Ser Ser Ser
         20
                            25
                                              30
Val Leu Asn His Ile Ser Ser Ser Ser Ser Ser Val Trp His Leu Phe
     35
                    40
                                       45
Asp Ile Cys Asp Ser Ser Lys Trp Asn Ala Tyr Cys Gln Val Trp Gly
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                     55
     <210> 123
     <211> 68
     <212> PRT
     <213> Human
     <400> 123
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Met Leu Thr Leu Pro Ile Leu Val Cys Lys Val Gln Asp Ser Asn Arg
Arg Lys Met Leu Pro Thr Gln Phe Leu Phe Leu Gly Val Leu Gly
         20
Ile Phe Gly Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp Gly Ser Thr
                         40'
     35
Gly Pro Thr Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe
                    55`
Ser Cys Leu Leu
     <210> 124
     <211> 110
     <212> PRT
     <213> mouse
     <400> 124
Met Ile Ser Pro Ala Trp Ser Leu Phe Leu Ile Gly Thr Lys Ile Gly
                           10
Leu Phe Phe Gln Val Ala Pro Leu Ser Val Val Ala Lys Ser Cys Pro
                             25
Ser Val Cys Arg Cys Asp Ala Gly Phe Ile Tyr Cys Asn Asp Arg Ser
      35
                         40
                                           45
Leu Thr Ser Ile Pro Val Gly Ile Pro Glu Asp Ala Thr Thr Leu Tyr
                                  60
  50
                    55.
Leu Gln Asn Asn Gln Ile Asn Asn Val Gly Ile Pro Ser Asp Leu Lys
                 70 ' 75
Asn Leu Leu Lys Val Gln Arg Ile Tyr Leu Tyr His Asn Ser Leu Asp
                          90
             85
Glu Phe Pro Thr Asn Leu Pro Lys Tyr Val Lys Glu Leu His
                             105
          100
     <210> 125
     <211> 330
     <212> PRT
     <213> mouse
     <400> 125
Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Ser Leu Pro Leu Leu
              5 10
Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala Cys Pro Cys Leu Arg
          20
                            25
Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe
      35
                        40
Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys .
                      55
                                        60
   50
Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser
                                   75
Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His
                                90
              85
                                                  95
Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr
                                               110
          100
                            105
```

Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu 120

Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu

Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala

135

115

130

140

125

```
150
                                  155
Ser Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser
                     170 • 175
          165
Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly Gly His Thr Val Asp
         180 . 185
                                   190
Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys Ile Glu Ala Ser Tyr
                             205
       195 200
Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser Trp
  210 · 215
                                    220
Pro Glu Ala Tyr Gly Ser Asp Phe Trp Gln Ser Ile Arg Phe Thr Asp 225 230 235 240
Tyr Ser Gln His Asn Gln Met Val Met Ala Leu Thr Leu Arg Cys Pro 245 250 255
Leu Lys Leu Glu Ala Ser Leu Cys Trp Arg Gln Asp Pro Leu Thr Pro 260 265 270
Cys Glu Thr Leu Pro Asn Ala Thr Ala Gln Glu Ser Glu Gly Trp Tyr
   275 280 285
Ile Leu Glu Asn Val Asp Leu His Pro Gln Leu Cys Phe Lys Phe Ser
 290 295 300
Phe Glu Asn Ser Ser His Val Glu Cys Pro His Gln Ser Gly Ser Leu 305 310 315 320
Pro Ser Trp Thr Val Ser Met Asp Thr Gln
           325
     <210> 126
     <211> 37
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     <213> Rat
     <400> 126
Met Leu Trp Val Leu Leu Ser Leu Thr Pro Leu Leu Ser Pro Leu Ile
              5
                             10
                                              15
Phe Phe Pro Val Lys Thr Val Ala Leu Glu Glu Ile Ser Thr Ile Cys
     20
Arg Ala Asp Val Leu
      35
     <210> 127
     <211> 42
     <212> PRT
   <213> mouse
     <400> 127
Met Gly Ser Pro Ile Ser Gly Val Cys Pro Val Leu Pro Gly Gly Leu
           5
                             10
                                               15
Phe Val Ala Leu Gly Trp Ile Phe Leu Leu Phe His Arg Asp Ala Phe
     20
                      25
Ser Leu His Thr Met Ser Ala Gly Phe Pro
     35
                        40
     <210> 128
     <211> 253
     <212> PRT
     <213> mouse
     <400> 128
Met Met Tyr Trp Ile Val Phe Ala Ile Phe Met Ala Ala Glu Thr Phe
```

```
10
1
Thr Asp Ile Phe Ile Ser Trp Ser Gly Pro Arg Ile Gly Arg Pro Trp
   20 25 30
Gly Trp Glu Gly Pro His His His His Leu Ala Ser Gly Ser His
     35 · 40
                            45
Lys Pro Leu Pro Leu Leu Thr His Arg Phe Pro Phe Tyr Tyr Glu Phe
                55
                             60
Lys Met Ala Phe Val Leu Trp Leu Leu Ser Pro Tyr Thr Lys Gly Ala
                       75
         70
Ser Leu Leu Tyr Arg Lys Phe Val His Pro Ser Leu Ser Arg His Glu
85 90 95
                           90
                                            -95
           85
Lys Glu Ile Asp Ala Cys Ile Val Gln Ala Lys Glu Arg Ser Tyr Glu
100 105 110
Thr Met Leu Ser Phe Gly Lys Arg Ser Leu Asn Ile Ala Ala Ser Ala
    115 120
                                     125
Ala Val Gln Ala Ala Thr Lys Ser Gln Gly Ala Leu Ala Gly Arg Leu
 130 135
                                  140
Arg Ser Phe Ser Met Gln Asp Leu Arg Ser Ile Pro Asp Thr Pro Val
145 150 155 160
Pro Thr Tyr Gln Asp Pro Leu Tyr Leu Glu Asp Gln Val Pro Arg Arg
       165 · 170 175
Arg Pro Pro Ile Gly Tyr Arg Pro Gly Gly Leu Gln Gly Ser Asp Thr
                                 190
                   185
         180
Glu Asp Glu Cys Trp Ser Asp Asn Glu Ile Val Pro Gln Pro Pro Val
195 200 205
Arg Pro Arg Glu Lys Pro Leu Gly Arg Ser Gln Ser Leu Arg Val Val 210 215 220
Lys Arg Lys Pro Leu Thr Arg Glu Gly Thr Ser Arg Ser Leu Lys Val
225 230 235 240
Arg Thr Arg Lys Lys Ala Met Pro Ser Asp Met Asp Ser
                   250
            245
     <210> 129
     <211> 40
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Met Lys Ala Met Ala Leu Ser Leu Gly Ala Ser Pro Val Leu Ala Phe
1 5 10
Leu Leu Ser Gly Tyr Ser Asp Gly Tyr Gln Val Cys Ser Arg Phe Gly
 20 25
Ser Lys Val Pro Gln Phe Leu Asn
      35
     <210> 130
     <211> 87
     <212> PRT
     <213> mouse
     <400> 130
Met Ile Ala Val Thr Phe Ala Ile Val Leu Gly Val Ile Ile Tyr Arg
                     10 15
Ile Ser Thr Ala Ala Ala Leu Ala Met Asn Ser Ser Pro Ser Val Arg
                    25 30
      20
Ser Asn Ile Arg Val Thr Val Thr Ala Thr Ala Val Ile Ile Asn Leu
```

40 ,

35

45

```
Val Val Ile Ile Leu Leu Asp Glu Val Tyr Gly Cys Ile Ala Arg Trp
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                                       60
Leu Thr Lys Ile Gly Glu Cys His Val Gln Asp Ser Ile Gly Ser Met
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                                  75
Gly Leu Gly Gln Gly Gln Pro
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     <210> 131
     <211> 70
     <212> PRT
     <213> mouse
     <400> 131
Met Phe Gly Leu Val His Val Cys Thr Cys Val Cys Val Cys
                             10
           . 5
Val Cys Val Cys Val Cys Ile Cys Ser Cys Gly Tyr Val His Val Pro
     20
                            25
Cys Gly Cys Val Cys Leu Trp Gly Pro Glu Val Arg Tyr Leu Pro Leu
                40
                                         45
     35
Ser Leu His Pro Gly Gly Phe Cys Phe Val Leu Phe Cys Phe Gly Pro 50 55 60
Gly Leu Ser Leu Ile Ser
65
     <210> 132
     <211> 63
     <212> PRT
     <213> mouse
  ` <400> 132
Met Trp Leu Leu Val Ala Leu Thr Leu Ser Val Tyr Ser Leu Val Ala
              5
                               10
Phe Val Thr Gly Met Leu Cys Asp Thr Val Val Ile Lys Met Leu Met
        20
                           25
                                             30
Ser Leu His Lys Ser Ser Lys Leu Asn Pro Arg Ala Lys Cys Gly Gly
                                         45
    35 40
Val Pro Leu Ile Pro Ala Leu Trp Gly Gln Val Gln Val Val Leu
. 50
                     55
     <210> 133
     <211> 39
     <212> PRT
     <213> mouse
     <400> 133
Met Asp Asn Thr Leu Ser Ile Ile Ile Tyr Leu Leu Phe Ile Phe Ala
           5 · 10 · 15
Ile Ser Val Leu Asp Ser Gln Leu Ser Thr Arg Cys Leu Trp Trp Phe
     20
                            25
                                              30
Ser Lys Asp Leu Glu Val Thr
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     <211> 90
     <212> PRT
     <213> Rat
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Met Pro Thr Met Trp Pro Leu Leu His Val Leu Trp Leu Ala Leu Val

<400> 134

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Cys Gly Ser Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala
Ala Ser Lys Thr Leu Leu Glu Lys Thr Gln Phe Ser Asp Lys Pro Val
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Gln Asp Arg Gly Leu Val Val Thr Asp Ile Lys Ala Glu Asp Val Val
                  55
                                       60
Leu Glu His Arg Ser Tyr Cys Ser Ala Arg Ala Arg Glu Arg Asn Phe 65 70 75 80
Ala Gly Glu Val Leu Gly Ile Cys His Ser
              85
     <210> 135
     <211> 193
     <212> PRT
     <213> Rat
     <400> 135
Met Thr Ser Gly Pro Gly Gly Pro Ala Ala Ala Thr Gly Gly Lys
                                10
Asp Thr His Gln Trp Tyr Val Cys Asn Arg Glu Lys Leu Cys Glu Ser
  20
                            25
                                               30
Leu Gln Ser Val Phe Val Gln Ser Tyr Leu Asp Gln Gly Thr Gln Ile
 35
                    40
Phe Leu Asn Asn Ser Ile Glu Lys Ser Gly Trp Leu Phe Ile Gln Leu 50 55 60
Tyr His Ser Phe Val Ser Ser Val Phe Thr Leu Phe Met Ser Arg Thr
65 70 75
Ser Ile Asn Gly Leu Leu Gly Arg Gly Ser Met Phe Val Phe Ser Pro
              85
                                90
Asp Gln Phe Gln Arg Leu Leu Lys Ile Asn Pro Asp Trp Lys Thr His
         100
                           105
Arg Leu Leu Asp Leu Gly Ala Gly Asp Gly Glu Val Thr Lys Ile Met 115 120 125
Ser Pro His Phe Glu Glu Ile Tyr Ala Thr Glu Leu Ser Glu Thr Met
                  135
130
                              140
Ile Trp Gln Leu Gln Lys Lys Lys Tyr Arg Val Leu Gly Ile Asn Glu
145 150 150 155
        150
Trp Gln Asn Thr Gly Phe Gln Tyr Asp Val Ile Ser Cys Leu Asn Leu \cdot 165 \cdot 170 \cdot 175
Leu Asp Arg Cys Asp Gln Pro Leu Thr Leu Leu Lys Asp Ile Arg Met
                             185
                                               190
Ser
     <210> 136
      <211> 106
      <212> PRT
      <213> Rat
     <400> 136
Met Ala Ala Pro Met Asp Arg Thr His Gly Gly Arg Ala Ala Arg Ala
                        10 ( 15
Leu Arg Arg Ala Leu Ala Leu Ala Ser Leu Ala Gly Leu Leu Leu Ser
           20
                              25
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Gly Leu Ala Gly Ala Leu Pro Thr Leu Gly Pro Gly Trp Arg Arg Gln
      35
                        40
Asn Pro Glu Pro Pro Ala Ser Arg Thr Arg Ser Leu Leu Leu Asp Ala
            55
 50
                                     60
Ala Ser Gly Gln Leu Arg Leu Glu Tyr Gly Phe His Pro Asp Ala Val 65 70 75 80
65
               70
                                   75
Ala Trp Ala Asn Leu Thr Asn Ala Ile Arg Glu Thr Gly Trp Ala Tyr
                             90
            85
Leu Asp Leu Gly Thr Asn Gly Ser Tyr Lys
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     <211> 286
     <212> PRT
     <213> Rat
     <400> 137
Met Ala Ala Ala Met Pro Leu Gly Leu Ser Leu Leu Leu Val Leu
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Val Gly Gln Gly Cys Cys Gly Arg Val Glu Gly Pro Arg Asp Ser Leu
        20
                          25
Arg Glu Glu Leu Val Ile Thr Pro Leu Pro Ser Gly Asp Val Ala Ala
      35
                        40
                                          45
Thr Phe Gln Phe Arg Thr Arg Trp Asp Ser Asp Leu Gln Arg Glu Gly
                                      60
 50
                  55
Val Ser His Tyr Arg Leu Phe Pro Lys Ala Leu Gly Gln Leu Ile Ser 65 70 75 80
                               75
                70
Lys Tyr Ser Leu Arg Glu Leu His Leu Ser Phe Thr Gln Gly Phe Trp
                    90
           85
Arg Thr Arg Tyr Trp Gly Pro Pro Phe Leu Gln Ala Pro Ser Gly Ala
          100
                         105
                                              110
Glu Leu Trp Val Trp Phe Gln Asp Thr Val Thr Asp Val Asp Lys Ser
                       120
  115
Trp Lys Glu Leu Ser Asn Val Leu Ser Gly Ile Phe Cys Ala Ser Leu
 130
                    135
                                       140
Asn Phe Ile Asp Ser Thr Asn Thr Val Thr Pro Thr Ala Ser Phe Lys
                                  155
                150
Pro Leu Gly Leu Ala Asn Asp Thr Asp His Tyr Phe Leu Arg Tyr Ala
165 170 175
            165
Val Leu Pro Arg Glu Val Val Cys Thr Glu Asn Leu Thr Pro Trp Lys
180 185 190
         180
Lys Leu Leu Pro Cys Ser Ser Lys Ala Gly Leu Ser Val Leu Leu Lys
     195 200
                                   205
Ala Asp Arg Leu Phe His Thr Ser Tyr His Ser Gln Ala Val His Ile
         215
                                     220
Arg Pro Ile Cys Arg Asn Ala His Cys Thr Ser Ile Ser Trp Glu Leu
        230
                                 235
Arg Gln Thr Leu Ser Val Val Phe Asp Ala Phe Ile Thr Gly Gln Gly
                               250
            245
Lys Lys Glu Ala Cys Pro Leu Ala Ser Gln Ser Leu Val Tyr Val Asp
                          265
                                              270
         260
Ile Thr Gly Tyr Ser Gln Asp Asn Glu Thr Leu Glu Val Ser
       275
                        280
                                 . 285
     <210> 138
     <211> 198
     <212> PRT
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PCT/NZ01/00099 WO 01/90357

<213> Rat

<400> 138 Met Thr Val Phe Arg Lys Val Thr Thr Met Ile Ser Trp Met Leu Leu Ala Cys Ala Leu Pro Cys Ala Ala Asp Pro Met Leu Gly Ala Phe Ala 20 25 Arg Arg Asp Phe Gln Lys Gly Gly Pro Gln Leu Val Cys Ser Leu Pro 35 40 45 Gly Pro Gln Gly Pro Pro Gly Pro Pro Gly Ala Pro Gly Ser Ser Gly 55 60 Met Val Gly Arg Met Gly Phe Pro Gly Lys Asp Gly Gln Asp Gly Gln 65 70 75 80 70 · 75 Asp Gly Asp Arg Gly Asp Ser Gly Glu Glu Gly Pro Pro Gly Arg Thr 85 90 Gly Asn Arg Gly Lys Gln Gly Pro Lys Gly Lys Ala Gly Ala Ile Gly 100 105 110 Arg Ala Gly Pro Arg Gly Pro Lys Gly Val Ser Gly Thr Pro Gly Lys 120 115 125 His Gly Ile Pro Gly Lys Lys Gly Pro Lys Gly Lys Lys Gly Glu Pro 130 135 140 Gly Leu Pro Gly Pro Cys Ser Cys Gly Ser Ser Arg Ala Lys Ser Ala 150 155 Phe Ser Val Ala Val Thr Lys Ser Tyr Pro Arg Glu Arg Leu Pro Ile 165 170 175 Lys Phe Asp Lys Ile Leu Met Asn Glu Gly Gly His Tyr Asn Ala Ser 185 180 Ser Gly Lys Phe Val Cys 195

<210> 139

<211> 233

<212> PRT

<213> Rat

<400> 139

Met Ala Ser Ala Leu Glu Glu Leu Gln Lys Asp Leu Glu Glu Val Lys ' 10 Val Leu Leu Glu Lys Ser Thr Arg Lys Arg Leu Arg Asp Thr Leu Thr 20 25 Asn Glu Lys Ser Lys Ile Glu Thr Glu Leu Arg Asn Lys Met Gln Gln 35 40 45Lys Ser Gln Lys Lys Pro Glu Phe Asp Asn Glu Lys Pro Ala Ala Val 55 Val Ala Pro Leu Thr Thr Gly Tyr Thr Val Lys Ile Ser Asn Tyr Gly 70 75 Trp Asp Gln Ser Asp Lys Phe Val Lys Ile Tyr Ile Thr Leu Thr Gly 85 90 95 Val His Gln Val Pro Ala Glu Asn Val Gln Val His Phe Thr Glu Arg 100 105 110 100 105 110 Ser Phe Asp Leu Leu Val Lys Asn Leu Asn Gly Lys Asn Tyr Ser Met 115 120 125 Ile Val Asn Asn Leu Leu Lys Pro Ile Ser Val Glu Ser Ser Ser Lys 130 135 140 Lys Val Lys Thr Asp Thr Val Ile Ile Leu Cys Arg Lys Lys Ala Glu 145 150 155 160

Asn Thr Arg Trp Asp Tyr Leu Thr Gln Val Glu Lys Glu Cys Lys Glu

170

```
Lys Glu Lys Pro Ser Tyr Asp Thr Glu Ala Asp Pro Ser Glu Gly Leu
180 185 190
Met Asn Val Leu Lys Lys Ile Tyr Glu Asp Gly Asp Asp Asp Met Lys
      195 200
                                  205
Arg Thr Ile Asn Lys Ala Trp Val Glu Ser Arg Glu Lys Gln Ala Arg 210 . 215 220
Glu Asp Thr Glu Phe Leu Gln Pro Gly
                  230
     <210> 140
     <211> 38
     <212> PRT
     <213> Human
     <400> 140
Met Gly Leu Ala Leu Cys Leu Ala Ser Ala Gly Ile Ser Gly Ser Arg
                             10
Ser Ala Phe Leu Gly Val Pro Arg Pro Arg Pro Thr Leu Ile Lys Leu
      20
                             25
Ile Asp Thr Val Asp Leu
      35
     <210> 141
     <211> 322
      <212> PRT
      <213> mouse
     <400> 141
Met Asp Ala Arg Trp Trp Ala Val Val Leu Ala Thr Leu Pro Ser
                                10
Leu Gly Ala Gly Gly Glu Ser Pro Glu Ala Pro Pro Gln Ser Trp Thr
                    25
     20
Gln Leu Trp Leu Phe Arg Phe Leu Leu Asn Val Ala Gly Tyr Ala Ser 35 40 45
Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Leu Arg Arg Lys Asn
                   55
Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys
                  70
                                  75
Val Phe Gly Asn Glu Pro Lys Ala Pro Asp Glu Val Leu Leu Ala Pro 85 90 95
Arg Thr Glu Thr Ala Glu Ser Thr Pro Ser Trp Gln Val Leu Lyş Leu 100 105 110
Val Phe Cys Ala Ser Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Ile
      115 120 125
Leu Gln Glu Arg Val Met Thr Gly Ser Tyr Gly Ala Thr Ala Thr Ser
130 135 140
Pro Gly Glu His Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg
145 150 155 160
Val Leu Ala Leu Val Val Ala Gly Leu Tyr Cys Val Leu Arg Lys Gln
             165 170 175
Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser
                             185
                                     . 190
          180
Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser
                        200 205
      195
Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met
                                        220
    210
                       215 .
```

Met Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr 230 235 225 Leu Thr Ala Gly Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser 255 245 250 Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu 260 265 270 265 260 Val Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp 275 280 285 Gln Asp Ala Leu Phe Ala Tyr Lys Met Ser Ser Val Gln Met Met Phe 300 290 295 Gly Val Asn Leu Phe Ser Cys Leu Phe Thr Val Gly Ser Leu Leu Glu 315 310 Gln Gly

> <210> 142 <211> 312 <212> PRT <213> mouse

<400> 142 Met Leu Cys Leu Cys Leu Tyr Val Pro Ile Ala Gly Ala Ala Gln Thr 10 5 Glu Phe Gln Tyr Phe Glu Ser Lys Gly Leu Pro Ala Glu Leu Lys Ser 25 20 Ile Phe Lys Leu Ser Val Phe Ile Pro Ser Gln Glu Phe Ser Thr Tyr 35 40 45 Arg Gln Trp Lys Gln Lys Ile Val Gln Ala Gly Asp Lys Asp Leu Asp 50 55 60 Gly Gln Leu Asp Phe Glu Glu Phe Val His Tyr Leu Gln Asp His Glu 65 70 75 Lys Lys Leu Arg Leu Val Phe Lys Ser Leu Asp Lys Lys Asn Asp Gly 90 Arg Ile Asp Ala Gln Glu Ile Met Gln Ser Leu Arg Asp Leu Gly Val 100 105 110 100 Lys Ile Ser Glu Gln Gln Ala Glu Lys Ile Leu Lys Ser Met Asp Lys 115 120 125 Asn Gly Thr Met Thr Ile Asp Trp Asn Glu Trp Arg Asp Tyr His Leu 135 140 130 Leu His Pro Val Glu Asn Ile Pro Glu Ile Ile Leu Tyr Trp Lys His 150 155 Ser Thr Ile Phe Asp Val Gly Glu Asn Leu Thr Val Pro Asp Glu Phe 165 170 175 Thr Val Glu Glu Arg Gln Thr Gly Met Trp Trp Arg His Leu Val Ala 185 190 180 Gly Gly Gly Ala Gly Ala Val. Ser Arg Thr Cys Thr Ala Pro Leu Asp 195 200 205 195 200 Arg Leu Lys Val Leu Met Gln Val His Ala Ser Arg Ser Asn Asn Met 210 215 220 Cys Ile Val Gly Gly Phe Thr Gln Met Ile Arg Glu Gly Gly Ala Lys 225 230 235 240 Ser Leu Trp Arg Gly Asn Gly Ile Asn Val Leu Lys Ile Ala Pro Glu 250 . 255 245 Ser Ala Ile Lys Phe Met Ala Tyr Glu Gln Met Lys Arg Leu Val Gly 260 265 270 Ser Asp Gln Glu Thr Leu Arg Ile His Glu Arg Leu Val Ala Gly Ser 285 280 .

PCT/NZ01/00099 WO 01/90357

```
Leu Ala Gly Ala Ile Ala Gln Ser Ser Ile Tyr Pro Met Glu Val Leu
   290
                      295
Lys Thr Arg Met Ala Leu Arg Lys
                  310
     <210> 143
     <211> 163
     <212> PRT
     <213> Rat
     <400> 143
Met Pro Leu Val Thr Thr Leu Phe Tyr Ala Cys Phe Tyr His Tyr Thr
1
                                10
                                                   15
Glu Ser Glu Gly Thr Phe Ser Ser Pro Val Asn Leu Lys Lys Thr Phe
     20
                             25
                                               30
Lys Ile Pro Asp Arg Gln Tyr Val Leu Thr Ala Leu Ala Ala Arg Ala
    . 35
                         40
Lys Leu Arg Ala Trp Asn Asp Val Asp Ala Leu Phe Thr Thr Lys Asn
                     55
Trp Leu Gly Tyr Thr Lys Lys Arg Ala Pro Ile Gly Phe His Arg Val
65
                  70
                                     75
Val Glu Ile Leu His Lys Asn Ser Ala Pro Val Gln Ile Leu Gln Glu
              85
                               90
                                                   95
Tyr Val Asn Leu Val Glu Asp Val Asp Thr Lys Leu Asn Leu Ala Thr
                             105
          100
                                                110
Lys Phe Lys Cys His Asp Val Val Ile Asp Thr Cys Arg Asp Leu Lys
      115
                          120
                                             125
Asp Arg Gln Gln Leu Leu Ala Tyr Arg Ser Lys Val Asp Lys Gly Ser
 130 135
                                       140
Ala Glu Glu Lys Ile Asp Val Ile Leu Ser Ser Gln Ile Arg
145
                 150
                                    155
Trp Lys Asn
     <210> 144
     <211> 330
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     <400> 144
Met Ala Gly Trp Ala Gly Ala Glu Leu Ser Val Leu Asn Pro Leu Arg
               5 .
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Ala Leu Trp Leu Leu Ala Ala Ala Phe Leu Leu Ala Leu Leu
          20
                              25
                                                 30
Gln Leu Ala Pro Ala Arg Leu Leu Pro Ser Cys Ala Leu Phe Gln Asp
       35
                          40
                                            45
Leu Ile Arg Tyr Gly Lys Thr Lys Gln Ser Gly Ser Arg Arg Pro Ala
                                        60
   50
                     55
Val Cys Arg Ala Phe Asp Val Pro Lys Arg Tyr Phe Ser His Phe Tyr
                                     75
65
                  70
                                                      80
Val Val Ser Val Leu Trp Asn Gly Ser Leu Leu Trp Phe Leu Ser Gln
              85
                                 90
Ser Leu Phe Leu Gly Ala Pro Phe Pro Ser Trp Leu Trp Ala Leu Leu
         100
                           105
                                                110
Arg Thr Leu Gly Val Thr Gln Phe Gln Ala Leu Gly Met Glu Ser Lys
```

120 Ala Ser Arg Ile Gln Ala Gly Glu Leu Ala Leu Ser Thr Phe Leu Val

125

```
1.35
Leu Val Phe Leu Trp Val His Ser Leu Arg Arg Leu Phe Glu Cys Phe
     150
                                   155
145
Tyr Val Ser Val Phe Ser Asn Thr Ala Ile His Val Val Gln Tyr Cys
                               170
            165
Phe Gly Leu Val Tyr Tyr Val Leu Val Gly Leu Thr Val Leu Ser Gln 180 185 190
       180
Val Pro Met Asn Asp Lys Asn Val Tyr Ala Leu Gly Lys Asn Leu Leu
                      200
                                  205
Leu Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Met Phe Phe Trp
 210
                  215
                                    220
Ser Ser Ala His Gln Tyr Lys Cys His Val Ile Leu Ser Asn Leu Arg
225 230 235 240
225 230 235 240
Arg Asn Lys Lys Gly Val Val Ile His Cys Gln His Arg Ile Pro Phe
245 250 255
Gly Asp Trp Phe Glu Tyr Val Ser Ser Ala Asn Tyr Leu Ala Glu Leu
                            265
                                             270
          260
Met Ile Tyr Ile Ser Met Ala Val Thr Phe Gly Leu His Asn Val Thr
 275 280
                                  285
Trp Trp Leu Val Val Thr Tyr Val Phe Phe Ser Gln Ala Leu Ser Ala 290 295 300
Phe Phe Asn His Arg Phe Tyr Lys Ser Thr Phe Val Ser Tyr Pro Lys
305 310 315
His Arg Lys Ala Phe Leu Pro Phe Leu Phe
       325
                                 330
     <210> 145
     <211> 301
     <212> PRT
     <213> Rat
     <400> 145
Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly
                              10
Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser
                                     . 30
          20 -
                            25
Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu
                                           45
     35
                         40
Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
                     55
                                      60
Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val
                 70
                                  75
Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile
             85 90
Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr
          100
                           105
                                               110
Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn
                       120
                                  . 125
     115
Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
130 135 140
                     135
Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu
                           . 155
                150
Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser
165 170 175
                             170
             165
Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe
                            185
           180
                                              190
```

Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp

```
195
                         200
Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser
               215
                                      220
 210
Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys
            230
                           235
Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu 245 250 255
             245
                             250
Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu
         260
                         265
                                      270
Gln Arg Cys Leu Leu Gly Leu Pro Val Trp Glu Gly Ser Pro His Leu
                     280
                                         285
      275
Pro Thr Gly His Trp Leu Arg Glu Leu Trp Ser Leu Leu
                     295
   290
     <210> 146
     <211> 61
     <212> PRT
     <213> Rat
     <400> 146
Met Glu Asn Ile Tyr Tyr Thr Asn Leu Ile Thr Ile Leu Gly Asn Lys
                             10
His Ala Asn Gln Met Glu Leu Asn Leu Gln Ala Leu Ile Leu Ser Pro
                          25
                                             30
     20
Trp Phe Ala Val Cys Ala Pro Pro Gly Phe Ala Arg Asp Gln Ala Val
    35 40
Arg Gly Leu Ala Leu Ala Gly Arg Arg Ile Thr Val Val
    50
      <210> 147
      <211> 105
      <212> PRT
      <213> Rat
     <400> 147
Met Leu Arg Arg Gln Leu Val Trp Trp His Leu Leu Ala Leu Leu Phe
                               10
 1 5
Leu Pro Phe Cys Leu Cys Gln Asp Glu Tyr Met Glu Ser Pro Gln Ala
                            25
                                              30
        20
Gly Gly Leu Pro Pro Asp Cys Ser Lys Cys Cys His Gly Asp Tyr Gly
                                         45
      35
                        40
Phe Arg Gly Tyr Gln Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Ile 50 55 60
Pro Gly Asn His Gly Asn Asn Gly Asn Asn Gly Ala Thr Gly His Glu
                70
                                 75
Gly Ala Lys Gly Glu Lys Gly Asp Lys Gly Asp Leu Gly Pro Arg Gly
                         90 . 95
             85
 Glu Arg Gly Gln His Gly Pro Lys Gly
           100
      <210> 148
      <211> 210
      <212> PRT
      <213> Rat
      <400> 148
```

Met Leu Gly Ala Thr Ser Leu Ser Trp Pro Trp Val Leu Trp Ala Val

```
Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu Gly Gly Leu
                              25
          20
                                                30
Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile Phe Tyr Ser
                          40
      35
Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly Met Ala Ile
                   55
Phe Ser Leu Leu Leu Gln Ala Leu Leu Leu Leu Pro Arg Leu Pro His
                 70
                                    75
Ala Pro Gly Ser Glu Gly Val Ser Ser Arg Ser Ala Arg Ile Ser Ser
              85
                                90
Asp Leu Leu Arg Asn Ile Val Pro Thr Arg Gln Leu Thr Arg Gln Thr
          100
                             105
His Leu Gln Thr Pro Leu Gln Ala Trp Arg Thr Arg Ala Lys Leu Pro
115 120 125
Pro Gly Gly Thr Glu Ala Val Pro Gly Arg Pro Gly Ala Gln Gln Asp
                                      140
  130 135
Ala Cys His Leu Leu Tyr Trp Thr Tyr Asn Gly Val Ser Ser Ile Pro
                                  155
         150
Cys His Arg Gly Gly Leu Ser His Val Pro Ser Glu Val Pro Ala Glu
165 170 175
Liys Ser Pro Val Leu Ile Leu His Ala Ala Pro Pro Phe Lys Thr Pro
     180 185 190
Val Asn Pro Trp Ala Arg Thr Val Val Gly Phe Phe Pro Ser Ser Pro
                          200
Ser Leu
  210
      <210> 149
      <211> 301
      <212> PRT
      <213> Rat
      <400> 149
Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly
                                  10
Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser
                             25
Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu
                          40
Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
                      55
Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val 65 70 75 80
Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile
                                  90
              85
Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr
                             105
          100
Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn
115 120 125
       115
Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
                      135
                                         140
Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu
                  150
                                 155
Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser
                                 170
               165
```

Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe

```
185
Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp
                      200
 195
                                          205
Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser
            215
                                      220
 210
Met Gly Met Arg His Arg Asp Arg Fro Thr Thr Gly Asn Thr Leu Lys 225 230 230 235
Ser Gly Leu Cys Ser Ala Leù Thr Thr Tyr Phe Phe Gly Ala Asp Leu 245 250 255
Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu 260 265 270
Pro Thr Gly His Trp Leu Arg Glu Leu Trp Ser Leu Leu
                    295
   290
     <210> 150
     <211> 80
     <212> PRT
     <213> Human
     <400> 150
Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys
1
                                10
Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu
 20
                       25
Phe Gln Asp Thr Lys Val Tyr Cys Thr Arg Glu Ser Asn Pro His Cys 35 40 45
 35
                      40
Gly Ser Asp Gly Gln Thr Tyr Gly Asn Lys Cys Ala Phe Cys Lys Ala
                    55
                                      60
Ile Val Lys Ser Gly Gly Lys Ile Ser Leu Lys His Pro Gly Lys Cys
                  70
     <210> 151
     <211> 27
     <212> PRT
     <213> mouse
     <400> 151
Met Leu Lys Ala Ser Leu His Ile Leu Phe Leu Gly Ile Leu Asn Val
            5
                        10
Pro Ile Val Asp Thr Ser Thr Lys Thr Gly Val
          20
                             25
     <210> 152
     <211> 86
<212> PRT
     <213> mouse
     <400> 152
Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile
                                10 ·
               5
Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser
      20
                        25
                                           30
Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala
       35
                    40
                                          45
Gly Ala Gln Gly Met Trp Gly Ile Trp Gly His Thr Ile Thr Cys Gly
```

```
Leu Ala Pro Gly Ala Lys Pro Cys Ser Leu Lys Arg Glu Gly Pro Asp
              70
Leu Leu Ser Phe Pro Pro
            85
     <210> 153
     <211> 72
     <212> PRT
     <213> mouse
     <400> 153
Met Ser Ala Ile Phe Asn Phe Gln Ser Leu Leu Thr Val Ile Leu Leu
                       10
Leu Ile Cys Thr Cys Ala Tyr Ile Arg Ser Leu Ala Pro Ser Ile Leu
                            25
Asp Arg Asn Lys Thr Gly Leu Leu Gly Ile Phe Trp Lys Cys Ala Arg
      35
                      40
                                            45
Ile Gly Glu Arg Lys Ser Pro Tyr Val Ala Ile Cys Cys Ile Val Met
                                         60
 50 55
Ala Phe Ser Ile Leu Phe Ile Gln
65
                  70
     <210> 154
     <211> 169
     <212> PRT
     <213> mouse
    <400> 154
Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly
              5
                                 10
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg
 20
                          25
Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly 35 40 45
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln
                 55
                                       60
Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu
                 70
                                     75
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr
             85
                                90
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly 100 105 110
                                               110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
    115
                      120
                                           125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu 130 135 140 .
                                140 ...
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145 150 155 160
Gly Glu Met Pro Pro Glu Asp Gly Met
     <210> 155
     <211> 61
     <212> PRT
     <213> mouse
```

```
<400> 155
Met Glu Lys Gln Met Asp Ala Ser Val Ser Val Ile Phe Gly Ser Ile
             5
                             10
Val Ile Ser Ala Phe Leu Tyr Leu Ser Leu Ala Gly Pro Trp Ala Val
        20
                          25
                                            30
Thr Val Thr Gln Met Arg Thr Ile Ile Ile Thr Met Asp Gln Leu Arg
     35
                        40
Asp Ala Leu Ile Leu Asp Gl'n Leu Lys Val Ala Val Ser
                     55
     <210> 156
     <211> 131
     <212> PRT
     <213> mouse
   · <400> 156
Met Ala Pro Ser Leu Trp Lys Gly Leu Val Gly Val Gly Leu Phe Ala
                            10
Leu Ala His Ala Ala Phe Ser Ala Ala Gln His Arg Ser Tyr Met Arg
     20 25
                                            30
Leu Thr Glu Lys Glu Asp Glu Ser Leu Pro Ile Asp Ile Val Leu Gln
                      40
                                          45
     35
Thr Leu Leu Ala Phe Ala Val Thr Cys Tyr Gly Ile Val His Ile Ala
                              60
 50 55
Gly Glu Phe Lys Asp Met Asp Ala Thr Ser Glu Leu Lys Asn Lys Thr 65 70 75 80
Phe Asp Thr Leu Arg Asn His Pro Ser Phe Tyr Val Phe Asn His Arg
           85 90
Gly Arg Val Leu Phe Arg Pro Ser Asp Ala Thr Asn Ser Ser Asn Leu
                           105
                                        110
        100
Asp Ala Leu Ser Ser Asn Thr Ser Leu Lys Leu Arg Lys Phe Asp Ser
     115
                        120
Leu Arg Arg
   130
   <210> 157
     <211> 133
     <212> PRT
     <213> mouse
     <400> 157
Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Leu Ala Leu Cys
                                10
                                                 15
              5
Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro 20 25 30
Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr 35 40 45
Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Glu His Val
                55
Gln Gly Thr Gly Ala Arg Ser Thr Ala Cys Thr Leu Ser Cys Arg Ala
                 70
                                   75
Pro Asn Ala Ser Ser Ser Gly Thr Met Pro Gly Thr Arg Ser Ala Gly
                               90
            85
Ser Thr Lys Asn Arg Val Asp Asp His Gly Lys Lys Asn Ser Arg Pro
                                    110
          100
                            105
Val Glu Arg Leu Gln Gln Arg Thr Leu Gln Ile Lys Ile Lys Ala Leu
```

120 .

```
Ser Phe Ser Gln Ala
   130
     <210> 158
     <211> 78
     <212> PRT
     <213> mouse
     <400> 158
Gly Thr Arg Lys Pro Leu Pro Met Glu Ala His Ser Arg Arg Glu Lys
                               10
Ala Ser Gly Leu Arg Leu Ala Trp His Tyr Glu Cys Ser Gly Val Ser
                                    30
    20 25
Val Trp Trp Met Cys Val Leu Gly Trp Leu Ser Phe Leu Val Phe Leu
     35
                       40
                                          45
Leu Phe Ser Leu Val Cys Ser Phe Pro Ser Pro Ile Asn His Ser His
                     55
                                   60
 50
Met Leu Pro Cys Leu Phe Leu Arg Gly Gly Gly Ser Asn Val
                  70
    <210> 159
     <211> 206
     <212> PRT
     <213> mouse
     <400> 159
Met Leu Pro Pro Ala Ile His Leu Ser Leu Ile Pro Leu Leu Cys Ile
1 5 10 15
Leu Met Arg Asn Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu
20 25 30
Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser
    35 40
                                         45
Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Ser Thr Gly 50 55 60
Leu Asp Arg Asn Ser Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser
65 70
Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys
             85
                                90
Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn
100 105 110
Trp Ile Gly Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser. 115 120 125
Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln
130 135 140
  130 135
Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val 145 150 150 160
Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Ser
165 170 175
His Asn Phe Glu Ser Val Ser Pro Ala Lys Pro Ala Gln His His Arg
     180 185 190
Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Leu Ser
                         200
                                             205
      <210> 160
      <211> 169
      <212> PRT
      <213> mouse
```

```
<400> 160
Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly
                               10
              5
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg
                           25
        20
Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly
     35 ` 40
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln
                  55
                                     60
Glu Leu Phe Asn Glu Tyr Gln. Phe Ser Val Asp Gln Leu Met Glu Leu 65 70 75 80
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr 85 90 95
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly
                  105 110
        100
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
                120
     115
                                125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
130 135 140
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145 150
                                  155
Gly Glu Met Pro Pro Glu Asp Gly Met
      165
     <210> 161
     <211> 114
     <212> PRT
     <213> mouse
     <400> 161
Met Ser Val Thr Ile Gly Arg Leu Ala Leu Phe Leu Ile Gly Ile Leu
                      10
Leu Cys Pro Val Ala Pro Ser Leu Thr Arg Ser Trp Pro Gly Pro Asp
     20
                           25
                                          30
Thr Cys Ser Leu Phe Leu Gln His Ser Leu Ser Leu Ser Leu Arg Leu
      35
                       40
                                         45
Gly Gln Ser Leu Glu Gly Gly Leu Ser Val Cys Phe His Val Cys Ile
   50
                    55
                                     60
His Ala Cys Glu Cys Val Ala Cys Cys Arg Val Leu Trp Asp Pro Lys 65 70 75 80
                 70
Pro Arg Gly Ser Ser Leu Cys Arg Trp Val Leu Gly Ser Ile Thr Cys
                       90 95
           85
Leu Phe Met Tyr Glu Val Gly Gly Trp Thr Gln Gly Gly Leu Ile Val
                            105
          100
```

<210> 162 <211> 46 <212> PRT

Ser Leu

<213> mouse

<400> 162

Met His Tyr Pro Cys Leu Ala Cys Leu Phe Val Asn Val His Trp Cys

1 5 10 15

Phe Ala Trp Met Cys Ile Leu Val Lys Met Ser Glu Leu Leu Glu Leu

```
25
Glu Leu Glu Thr Met Val Ser Cys Leu Val Asp Val Gly Asn
    35 40 45
    <210> 163
    <211> 122
    <212> PRT
    <213> mouse
    <400> 163
Met Phe Thr Phe Val Val Leu Val Ile Thr Ile Val Ile Cys Leu Cys
          5 . 10
His Val Cys Phe Gly His Phe Lys Tyr Leu Ser Ala His Asn Tyr Lys
       20 25
Ile Glu His Thr Glu Thr Asp Ala Val Ser Ser Arg Ser Asn Gly Arg
     35
                     40
                                     45
Pro Pro Thr Ala Gly Ala Val Pro Lys Ser Ala Lys Tyr Ile Ala Gln
               55
 50
                                60
Val Leu Gln Asp Ser Glu Gly Asp Gly Asp Gly Asp Gly Ala Pro Gly 65 70 75 80
        70
                            75
Ser Ser Gly Asp Glu Pro Pro Ser Ser Ser Ser Gln Asp Glu Glu Leu
         85 90 95
Leu Met Pro Pro Asp Gly Leu Thr Asp Thr Asp Phe Gln Ser Cys Glu
       100 105
Asp Ser Leu Ile Glu Asn Glu Ile His Gln
    115 120
    <210> 164
    <211> 60
     <212> PRT
    <213> Rat
    <400> 164
Met Ser Phe Val Lys Ile Glu Ala Thr Pro Thr Gln Thr Lys Trp Pro
                  10
1 . 5
                                      15
Phe Ser Val Val Pro Gln Ser Leu Leu Val Thr Val Tyr Ile Cys Tyr
    20
                       25
Ile Phe Leu Val Ile Phe Phe Phe Phe Phe Glu Ala Cys Gln Glu Val
   35
                  40
Leu Cys Ser Phe Phe Asp Phe Ser Arg Arg Arg Gly
   50
                  55
    <210> 165
     <211> 57
     <212> PRT
    <213> mouse
    <400> 165
Met Gly Ser Pro Ile Ser Gly Val Cys Pro Val Leu Pro Gly Gly Leu 1 5 10 15
Phe Val Ala Leu Gly Trp Ile Phe Leu Leu Phe His Arg Asp Ala Phe
   20
                25 30
Ser Leu His Thr Met Ser Ala Gly Phe Pro Lys Ser Pro Ala Asn Pro
 35 40
His His Pro Pro Leu Arg Leu Ser Pro
   50
                   55
```

```
<210> 166
    <211> 75
    <212> PRT
    <213> mouse
    <400> 166
Lys Thr Arg Arg Thr Leu Thr Gly Gln Leu Gly Leu Phe Ser Val Asp
          5 ` 10
1.
Phe Met Val Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro
 20
                      25
                                   30
Phe Pro Leu Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys
 35 40
                             45
Gln Trp Glu Gly Ser Thr Met Thr His Thr His Thr His Thr His Ile
      55
His Ile His Thr Pro Pro Arg Gln Cys Gln Ser
             70
    <210> 167
    <211> 52
    <212> PRT
    <213> mouse
    <400> 167
Val Arg Ser Leu Glu Gln Leu Gly Leu Phe Ser Val Asp Phe Met Val
          5
                           10
                                          15
Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro Phe Pro Leu
   20 25
                                  30
Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys Gln Trp Glu
 35
             . 40
                                    45
Gly Ser Thr Met
  50
    <210> 168
    <211> 119
    <212> PRT
    <213> Rat
   <400> 168
Met Leu Gly Ala Thr Ser Leu Ser Trp Pro Trp Val Leu Trp Ala Val
          5
                   10
Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu Gly Gly Leu
                               , 30
   20 25
Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile Phe Tyr Ser
    35 40 45
Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly Met Ala Ile
                 55
                        . 60
Phe Ser Leu Leu Leu Gln Ala Leu Leu Leu Pro Arg Leu Pro His
       70 75
Ala Pro Gly Ser Glu Gly Val Ser Ser Arg Ser Ala Arg Ile Ser Ser
          85
                        90 95
Asp Leu Leu Arg Asn Ile Val Pro Thr Arg Gln Leu Thr Arg Gln Thr
   100
                        105
His Leu Gln Thr Pro Leu Gln
     115
    <210> 169
    <211> 104
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<212> PRT
     <213> Rat
     <220>
     <400> 169
Leu Val Pro Lys Ser Ala Arg Ala Ser Leu Leu Cys Cys Gly Pro Lys
                                 10
Leu Ala Ala Cys Gly Ile Val Leu Ser Ala Trp Gly Val Ile Met Leu
        20
                            25
                                              30
Ile Met Leu Gly Ile Phe Phe Asn Val His Ser Ala Val Xaa Ile Xaa
      35
                        40
                                           45
Asp Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile
 50
                    55
                                       60
Tyr Asn Leu Tyr Glu Gln Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly
                                   75
        70
Leu Tyr Leu Leu Xaa Gly Gly Phe Ser Phe Cys Gln Val Arg Leu Asn
       85
                                 90
Lys Arg Lys Glu Tyr Met Val Arg
      100
     <210> 170
     <211> 123
     <212> PRT
     <213> Rat
     <220>
     <221> UNSURE
     <222> (27)...(27)
     <221> UNSURE
     <222> (104)...(104)
     <221> UNSURE
     <222> (118) ... (118)
     <400> 170
Met Arg Pro Gly Ala Asp Trp Ala Ala Val Cys Ala Leu Trp Pro Ser
              5
                              10
Trp Arg Pro Ser Cys Ser Leu Pro Ser Ser Xaa Arg Ile Gln Pro Asp
      20
                           25
Glu Leu Trp Leu Tyr Arg Asn Pro Tyr Val Lys Ala Glu Tyr Phe Pro
     35
                        40
                                           45
Thr Gly Pro Met Phe Val Ile Ala Phe Leu Thr Pro Leu Ser Leu Ile
  50 55
                                     60
Phe Phe Ala Lys Phe Leu Arg Lys Ala Asp Ala Asp Arg Gln Arg Ala 65 70 75 80
Ser Leu Pro Arg Cys Gln Pro Cys Pro Ser Ala Lys Trp Cys Leu Tyr
            85
                              90
Gln His His Lys Thr Asp Ser Xaa Gln Gly His Ala Gln Ile Ala Ser
         100
                            105
Thr Glu Cys Ser Pro Xaa Gly Ile Ala His Ser
       115
                         120
     <210> 171
     <211> 75
```

<212> PRT <213> Rat <400> 171 Ser Ala Gly Val Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile 10 Ala Phe Gly Pro Ala Leu Ser Leu Tyr Val Phe Thr Ile Ala Thr Asp 20 . 25 30 20 25 30 Pro Leu Arg Val Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val 35 40 Ser Leu Leu Ser Ser Val Phe Trp Phe Leu Val Arg Val Ile Thr 55 Asp Asn Arg Asp Gly Pro Val Gln Asn Tyr Leu 65 70 <210> 172 <211> 79 <212> PRT <213> Human <400> 172 . Lys Thr Ser Tyr His Tyr His Thr Asn Val Glu Glu Leu Thr Ile Pro 1 5 . 10 Glu Thr Arg Asn Asn Leu Tyr Ile Ser Ile Ser Trp Leu Trp Cys Leu 20 25 30 Val Leu Val Leu Leu Ser Thr Met Ile Leu Asn Lys His Gly Trp Met 35 40 45 Lys Ala Asn Ala Tyr Ser Leu Val Pro Ser Ile Ile Tyr Ser Pro Ser 50 55 60 Tyr Leu Lys Leu Leu Leu Arg Leu Tyr Lys Leu Gln Ile Cys Cys . 70 <210> 173 <211> 134 <212> PRT <213> Human <220> <400> 173 Leu Arg Gly Arg Gly Val Cys Ser Gln Glu Ser Phe Gly Gly 5 10 Cys Cys Val Ser Gly Leu Ile Ala Met Gly Thr Lys Ala Gln Val Glu 20 25 30 35 40 45 55 60 ...

Arg Lys Leu Cys Leu Phe Ile Leu Ala Ile Leu Leu Cys Ser Leu Ala Leu Gly Ser Val Thr Val His Ser Ser Glu Pro Glu Val Arg Ile Pro Glu Asn Asn Pro Val Lys Leu Ser Cys Ala Tyr Ser Gly Phe Ser 70 75 Ser Pro Arg Val Glu Trp Lys Phe Asp Gln Gly Asp Thr Thr Arg Leu 85 90 95 Val Cys Tyr Asn Asn Lys Ile Thr Ala Ser Tyr Glu Asp Arg Val Thr 105 100 110 Phe Leu Pro Thr Gly Ile Thr Phe Lys Ser Val Thr Arg Glu Asp Thr 115 120 125 Gly Thr Tyr Thr Cys Met 130

```
<210> 174
     <211> 137
     <212> PRT
     <213> Human
     <400> 174
Ala Trp Ser Arg Pro Arg Tyr Asp Ser Val Leu Ala Leu Ser Ala Ala
             5
                              10
Leu Gln Ala Thr Arg Ala Leu Met Val Val Ser Leu Val Leu Gly Phe
                      25
    20
                                      30
Leu Ala Met Phe Val Ala Thr Met Gly Met Lys Cys Thr Arg Cys Gly
    35
                     40
                                       45
Gly Asp Asp Lys Val Lys Lys Ala Arg Ile Ala Met Gly Gly Ile
                  55
                            60
Ile Phe Ile Val Ala Gly Leu Ala Ala Leu Val Ala Cys Ser Trp Tyr
                               75.
                70
Gly His Gln Ile Val Thr Asp Phe Tyr Asn Pro Leu Ile Pro Thr Asn
            85
                            90
Ile Lys Tyr Glu Phe Gly Pro Ala Ile Phe Ile Gly Trp Ala Gly Ser
Ala Leu Val Ile Leu Gly Gly Ala Leu Ser Pro Val Pro Val Leu Gly
   115 120
Ile Arg Ala Gly Leu Gly Thr Cys Pro
  130
                    135
     <210> 175
     <211> 43
     <212> PRT
     <213> Human
    <400> 175
Met Lys Leu Ser Gly Met Phe Leu Leu Ser Leu Ala Leu Phe Cys
            5 10
Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu
 20 25
                                            30
Ser Arg Thr Pro Arg Pro Thr Ala Leu Gly Asn
. 35
                      40
     <210> 176
     <211> 63
     <212> PRT
     <213> Rat
    <400> 176
Pro Asn Thr Arg Pro Arg Arg His Thr Ala Cys Arg Val Ser Ile Ser
             5 10 . 15
Val Phe Tyr Met Leu His Thr Glu Leu Lys Lys Cys Trp Phe Phe Leu 20 25 30
Phe Cys Phe Ser Leu Phe Leu Trp Phe Cys Phe Trp Phe Cys Phe Leu
     35
                      40
                                      45
Leu Pro Arg Phe Asp Tyr Leu Pro Met Pro Ser Thr Arg Pro Arg
  50
                    55
    <210> 177
   <211> 52
   <212> PRT
```

<213> mouse

<400> 177 Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile 5 10 Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser 20 25 Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala 40 . 35 45 Gly Ala Gln Gly 50 <210> 178 <211> 62 <212> PRT <213> mouse <400> 178 Val Ser Pro Arg Pro Thr Tyr Pro Ser Thr Ala Ser Ser Met Ala Ala 1 5 10 Phe Leu Val Thr Gly Phe Phe Phe Ser Leu Phe Val Val Leu Gly Met 25 20 30 Glu Pro Arg Ala Leu Phe Arg Pro Asp Lys Ala Leu Pro Leu Ser Cys 35 40 45 Ala Lys Pro Thr Ser Leu Cys Val Gln Ser Ser Phe Leu Gly 55 <210> 179 <211> 123 <212> PRT <213> mouse <400> 179 Ala Ser Arg Thr Ala Val Met Ser Leu Cys Arg Cys Gln Gln Gly Ser 1 5 10 Arg Ser Arg Met Asp Leu Asp Val Val Asn Met Phe Val Ile Ala Gly 20 25 30 Gly Thr Leu Ala Ile Pro Ile Leu Ala Phe Val Ala Ser Phe Leu Leu 35 40 Trp Pro Ser Ala Leu Ile Arg Ile Tyr Tyr Trp Tyr Trp Arg Arg Thr 50 55 60 Leu Gly Met Gln Val Arg Tyr Ala His His Glu Asp Tyr Gln Phe Cys 70 75 Tyr Ser Phe Arg Gly Arg Pro Gly His Lys Pro Ser Ile Leu Met Leu 90 85 His Gly Phe Ser Ala His Lys Gly His Val Ala Gln Arg Gly Gln Val Pro Ser Arg Lys Asn Leu His Phe Gly Cys Val 115 120 <210> 180 <211> 120 <212> PRT <213> mouse <220> <221> UNSURE

<222> (5)...(5) <400> 180 Ala Arg Arg Arg Xaa Arg Trp Arg Arg Gly Cys Cys Trp Leu Ile Gly 1 5 10 15 Thr Gly Leu Arg Ala Ala Thr Trp Thr Val Leu Cys Ser Pro Asn Ser 20 25 30 Ser Leu Val Val Ala Arg His Thr Lys Ser Phe Pro Pro Lys Lys Pro 35 40 45 Leu Gln Ala Leu Thr Met Ser Ile Met Asp His Ser Pro Thr Thr Gly 55 . 60 . Val Val Thr Val Ile Val Ile Leu Ile Ala Ile Ala Ala Leu Gly Gly 65 70 75 80 Leu Ile Leu Gly Cys Trp Cys Tyr Leu Arg Leu Gln Arg Ile Ser Gln 85 90 Ser Glu Asp Glu Glu Ser Ile Val Gly Asp Gly Glu Thr Lys Glu Pro 100 105 Phe Tyr Trp Cys Ser Thr Leu Leu 115 <210> 181 <211> 60 <212> PRT <213> mouse <400> 181 Lys Gly Pro Glu Val Ser Cys Cys Ile Lys Tyr Phe Ile Phe Gly Phe 1 5 10 15 Asn Val Ile Phe Trp Phe Leu Gly Ile Thr Phe Leu Gly Ile Gly Leu 20 25 Trp Ala Trp Asn Glu Lys Gly Val Leu Ser Asn Ile Ser Ser Ile Thr 35 40 45 Asp Leu Gly Gly Phe Asp Pro Val Trp Leu Phe Leu 55 <210> 182 <211> 72 <212> PRT <213> mouse <220> <400> 182 Lys Pro Thr Val Gly Ser Ala Glu Val Ala Ile Ala Val Phe Leu Val . 10 Ile Cys Ile Ile Val Val Leu Thr Ile Leu Gly Tyr Cys Phe Phe Lys 20 25 30 Asn Gln Arg Lys Glu Phe His Ser Pro Leu His His Pro Pro Pro Thr 35 40 45

Pro Ala Ser Ser Thr Val Ser Thr Thr Glu Asp Thr Glu His Leu Val

55

<210> 183 <211> 771

50

Tyr Asn His Thr Thr Gln Pro Leu

60

<212> PRT <213> Rat

<220>

<400> 183 Glu Leu Tyr Leu Asp Gly Asn Gln Phe Thr Leu Val Pro Lys Glu Leu 10 Ser Asn Tyr Lys His Leu Thr Leu Ile Asp Leu Ser Asn Asn Arg Ile 25 Ser Thr Leu Ser Asn Gln Ser Phe Ser Asn Met Thr Gln Leu Leu Thr 35 40 Leu Ile Leu Ser Tyr Asn Arg Leu Arg Cys Ile Pro Pro Arg Thr Phe 50 55 . 60 Asp Gly Leu Lys Ser Leu Arg Leu Leu Ser Leu His Gly Asn Asp Ile 65 70 75 80 Ser Val Val Pro Glu Gly Ala Phe Gly Asp Leu Ser Ala Leu Ser His 85 90 95 Leu Ala Ile Gly Ala Asn Pro Leu Tyr Cys Asp Cys Asn Met Gln Trp 100 105 110 Leu Ser Asp Trp Val Lys Ser Glu Tyr Lys Glu Pro Gly Ile Ala Arg 115 120 125 115 120 Cys Ala Gly Pro Gly Glu Met Ala Asp Lys Leu Leu Leu Thr Thr Pro 130 135 140 Ser Lys Asn Phe Thr Cys Gln Gly Pro Val Asp Val Thr Ile Gln Ala 145 150 150 160 Lys Cys Asn Pro Cys Leu Ser Asn Pro Cys Lys Asn Asp Gly Thr Cys 165 170 175 Asn Asn Asp Pro Val Asp Phe Tyr Arg Cys Thr Cys Pro Tyr Gly Phe 180 185 190 Lys Gly Gln Asp Cys Asp Val Pro Ile His Ala Cys Thr Ser Asn Pro 195 200 205 205 Cys Lys His Gly Gly Thr Cys His Leu Lys Pro Arg Arg Glu Thr Trp 210 215 220 Ile Trp Cys Thr Cys Ala Asp Gly Phe Glu Gly Glu Ser Cys Asp Ile 225 230 235 240 Asn Ile Asp Asp Cys Glu Asp Asn Asp Cys Glu Asn Asn Ser Thr Cys 245 250 255 Val Asp Gly Ile Asn Asn Tyr Thr Cys Leu Cys Pro Pro Glu Tyr Thr 260 265 270 Gly Glu Leu Cys Glu Glu Lys Leu Asp Phe Cys Ala Gln Asp Leu Asn 275 280 . Pro Cys Gln His Asp Ser Lys Cys Ile Leu Thr Pro Lys Gly Phe Lys 290 295 300 295 300 Cys Asp Cys Thr Pro Gly Tyr Ile Gly Glu His Cys Asp Ile Asp Phe 305 310 315 320 Asp Asp Cys Gln Asp Asn Lys Cys Lys Asn Gly Ala His Cys Thr Asp 325 330 335 Ala Val Asn Gly Tyr Thr Cys Val Cys Pro Glu Gly Tyr Ser Gly Leu 340 345 350 Phe Cys Glu Phe Ser Pro Pro Met Val Phe Leu Arg Thr Ser Pro Cys 360 365 Asp Asn Phe Asp Cys Gln Asn Gly Ala Gln Cys Ile Ile Arg Val Asn 375 380 Glu Pro Ile Cys Gln Cys Leu Pro Gly Tyr Leu Gly Glu Lys Cys Glu 390

Lys Leu Val Ser Val Ser Ile Leu Val Asn Lys Glu Ser Tyr Leu Gln

410

405

```
Ile Pro Ser Ala Lys Val Arg Pro Gln Thr Asn Ile Thr Leu Gln Ile
                          425
        420
                                          430
Ala Thr Asp Glu Asp Ser Gly Ile Leu Leu Tyr Lys Gly Asp Lys Asp 435 440 445
His Ile Ala Val Glu Ser Ile Glu Gly Ile Arg Ala Ser Tyr Asp Thr
                  455
                                   460
Gly Ser His Pro Ala Ser Ala Ile Tyr Ser Val Glu Thr Ile Asn Asp
465
         470
                               475
Gly Asn Phe His Ile Val Glu Leu Leu Thr Leu Asp Ser Ser Leu Ser 485 490 495
Leu Ser Val Asp Gly Gly Ser Pro Lys Ile Ile Thr Asn Leu Ser Lys
       500 505
Gln Ser Thr Leu Asn Phe Asp Ser Pro Leu Tyr Val Gly Met Pro
                       520
     515
                                       525
Gly Lys Asn Asn Val Ala Ser Leu Arg Gln Ala Pro Gly Gln Asn Gly
           535 540
  530
Thr Ser Phe His Gly Cys Ile Arg Asn Leu Tyr Ile Asn Ser Glu Leu 545 550 550 555 560
       550
                                555
Gln Asp Phe Arg Lys Val Pro Met Gln Thr Gly Ile Leu Pro Gly Cys
           565
                            570
                                      575
Glu Pro Cys His Lys Lys Val Cys Ala His Gly Thr Cys Gln Pro Ser
         580
                           585
                                            590
Ser Gln Ser Gly Phe Thr Cys Glu Cys Glu Glu Gly Trp Met Gly Pro
                     600
                                       605
Leu Cys Asp Gln Arg Thr Asn Asp Pro Cys Leu Gly Asn Lys Cys Val
 610
           615
                                620
His Gly Thr Cys Leu Pro Ile Asn Ala Phe Ser Tyr Ser Cys Lys Cys
              630
                     635
Leu Glu Gly His Gly Gly Val Leu Cys Asp Glu Glu Glu Asp Leu Phe
            645
                             650
                                               655
Asn Pro Leu Pro Gly Asp Gln Val Gln Ala Arg Glu Val Gln Ala Leu
       660
                        665
                                     670
Trp Ala Arg Ala Ala Leu Leu Trp Met Gln Gln Trp Ile His Arg Gly
  675 680 685
Gln Leu Thr Gln Arg Ile Ser Cys Arg Gly Glu Arg Ile Arg Asp Tyr
. 690
                    695
                                   700
Tyr Gln Ser Ser Arg Val Arg Cys Leu Ser Asn Asp
     <210> 184
    <211> 340
     <212> PRT
     <213> mouse
     <400> 184
Asp Gly Ser Leu Trp Leu Gln Ala Thr Gln Pro Asp Asp Ala Gly His
                              10
Tyr Thr Cys Val Pro Ser Asn Gly Phe Leu His Pro Pro Ser Ala Ser
   20
                           25
                                           30
```

Ala Tyr Leu Thr Val Leu Tyr Pro Ala Gln Val Thr Val Met Pro Pro

Glu Thr Pro Leu Pro Thr Gly Met Arg Gly Val Ile Arg Cys Pro Val

Arg Ala Asn Pro Pro Leu Leu Phe Val Thr Trp Thr Lys Asp Gly Gln 65 70 75 80 Ala Leu Gln Leu Asp Lys Phe Pro Gly Trp Ser Leu Gly Pro Glu Gly

40

· 35

50 55

45

```
Ser Leu Ile Ile Ala Leu Gly Asn Glu Asp Ala Leu Gly Glu Tyr Ser
                        105
          100
                                             110
Cys Thr Pro Tyr Asn Ser Leu Gly Thr Ala Gly Pro Ser Pro Val Thr
             120
Arg Val Leu Leu Lys Ala Pro Pro Ala Phe Ile Asp Gln Pro Lys Glu
130 135 140
Glu Tyr Phe Gln Glu Val Gly Arg Glu Leu Leu Ile Pro Cys Ser Ala
                           155
      150
Arg Gly Asp Pro Pro Pro Ile Val Ser Trp Ala Lys Val Gly Arg Gly
                     170
         165
                                                175
Leu Gln Gly Gln Ala Gln Val Asp Ser Asn Asn Ser Leu Val Leu Arg
180 185 190
                           185
                                          190
Pro Leu Thr Lys Glu Ala Gln Gly Arg Trp Glu Cys Ser Ala Ser Asn
     195
                      200
                                205
Ala Val Ala Arg Val Thr Thr Ser Thr Asn Val Tyr Val Leu Gly Thr
                    215
  210
                                     220
Ser Pro His Val Val Thr Asn Val Ser Val Val Pro Leu Pro Lys Gly
        230
Ala Asn Val Ser Trp Glu Pro Gly Phe Asp Gly Gly Tyr Leu Gln Arg
245 250 255
Phe Ser Val Trp Tyr Thr Pro Leu Ala Lys Arg Pro Asp Arg Ala His
    260 265
His Asp Trp Val Ser Leu Ala Val Pro Ile Gly Ala Thr His Leu Leu
    275 280
                                       285
Val Pro Gly Leu Gln Ala His Ala Gln Tyr Gln Phe Ser Val Leu Ala
290 295 300
Gln Asn Lys Leu Gly Ser Gly Pro Phe Ser Glu Ile Val Leu Ser Ile
305 310 315 320
Pro Glu Gly Leu Pro Thr Thr Pro Ala Ala Pro Gly Leu Pro Ala Thr
          325
                              330
Arg Ser Arg Val
         340
     <210> 185
     <211> 536
     <212> PRT
     <213> mouse
     <400> 185
Lys Val Glu Gly Glu Gly Arg Gly Arg Trp Ala Leu Gly Leu Leu Arg
1
                       10
Thr Phe Asp Ala Gly Glu Phe Ala Gly Trp Glu Lys Val Gly Ser Gly
         20
                           25
Gly Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp 35 40 45 .
Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg
   50 55
                                    60
Met Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg
65 70
                                 75
Tyr Ile Leu Pro Val Tyr Gly Ile Cys Gln Glu Pro Val Gly Leu Val
             85
                              90
Met Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu
                  105
Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val 115 120 125
```

Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp

```
130
                    135
Leu Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr Gln Met Ser Arg
                         155
       150
Phe Leu Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His 165 170 175
                                                175
Asp Leu Ser Met Asp Gly Leu Phe Gly Thr Ile Gly Tyr Leu Pro Pro
   180 185 190
Glu Arg Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val
                       200
      195
                                       205
Tyr Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Asn Asn Pro
           215
                                    220
Phe Ala Asp Glu Lys Asn Ile Leu His Ile Met Met Lys Val Val Lys 225 230 230 235
Gly His Arg Pro Glu Leu Pro Pro Ile Cys Arg Pro Arg Pro Arg Ala 245 250 255
Cys Ala Ser Leu Ile Gly Leu Met Gln Arg Cys Trp His Ala Asp Pro
         260
                           265
                                            270
Gln Val Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu
275 280 285
Cys Glu Lys Pro Asp Glu Glu Val Lys Asp Leu Ala His Glu Pro Gly
 290 295
                                    300
Glu Lys Ser Ser Leu Glu Ser Lys Ser Glu Ala Arg Pro Glu Ser Ser
305 310
                                 315
Arg Leu Lys Arg Ala Ser Ala Pro Pro Phe Asp Asn Asp Cys Ser Leu
        325 330 335
Ser Glu Leu Ser Gln Leu Asp Ser Gly Ile Phe Pro Arg Leu Leu 340 345 350
Lys Gly Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Cys Lys Leu Pro 355 360 365
Ser Ser Ser Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser
 370
                  375
Ala Phe Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg Glu Ala 385 390 395 400
Ser Thr Gly Asp Leu Gly Pro Thr Asp Ile Gln Lys Lys Lys Leu Val
405 410 415
Asp Ala Ile Ile Ser Gly Asp Thr Ser Arg Leu Met Lys Ile Leu Gln
                        425
                                . 430
       420
Pro Gln Asp Val Asp Leu Val Leu Asp Ser Ser Ala Ser Leu Leu His
     435 440 445
Leu Ala Val Glu Ala Gly Gln Glu Glu Cys Val Lys Trp Leu Leu
           455 460
Asn Asn Ala Asn Pro Asn Leu Thr Asn Arg Lys Gly Ser Thr Pro Leu
               470
                                475
His Met Ala Val Glu Arg Lys Gly Arg Gly Ile Val Glu Leu Leu
           485
                           490
Ala Arg Lys Thr Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Aļa
        500 505
                                            , 510
Leu His Phe Ala Ala Gln Asn Gly Asp Glu Gly Gln His Lys Ala Ala
    515
              520
                                          525
Ala Arg Glu Glu Cys Phe Cys Gln
   530
     <210> 186
     <211> 337
     <212> PRT
```

<213> Rat

<220>

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<400> 186
Arg Phe Gly Tyr Gln Met Asp Glu Gly Asn Gln Cys Val Asp 1 5 10
 Val Asp Glu Cys Ala Thr Asp Ser His Gln Cys Asn Pro Thr Gln Ile
20 25 30
 Cys Ile Asn Thr Glu Gly Gly Tyr Thr Cys Ser Cys Thr Asp Gly Tyr 35
                        40
                                              45
 Trp Leu Leu Glu Gly Gln Cys Leu Asp Ile Asp Glu Cys Arg Tyr Gly 50 55 60
 Tyr Cys Gln Gln Leu Cys Ala Asn Val Pro Gly Ser Tyr Ser Cys Thr 65 70 75 . 80
 Cys Asn Pro Gly Phe Thr Leu Asn Asp Asp Gly Arg Ser Cys Gln Asp
              85
                                   90
 Val Asn Glu Cys Glu Thr Glu Asn Pro Cys Val Gln Thr Cys Val Asn
                      105 110
           100
 Thr Tyr Gly Ser Phe Ile Cys Arg Cys Asp Pro Gly Tyr Glu Leu Glu
115 120 125
 Glu Asp Gly Ile His Cys Ser Asp Met Asp Glu Cys Ser Phe Ser Glu
                      135 140
 Phe Leu Cys Gln His Glu Cys Val Asn Gln Pro Gly Ser Tyr Phe Cys 145 150 155 160
 Ser Cys Pro Pro Gly Tyr Val Leu Leu Glu Asp Asn Arg Ser Cys Gln
165 170 175
 Asp Ile Asn Glu Cys Glu His Arg Asn His Thr Cys Thr Pro Leu Gln
180 185 190
 Thr Cys Tyr Asn Leu Gln Gly Gly Phe Lys Cys Ile Asp Pro Ile Val
195 200 205
 Cys Glu Glu Pro Tyr Leu Leu Ile Gly Asp Asn Arg Cys Met Cys Pro
210 215 220
Ala Glu Asn Thr Gly Cys Arg Asp Gln Pro Phe Thr Ile Leu Phe Arg 225 230 235 240
 Asp Met Asp Val Val Ser Gly Arg Ser Val Pro Ala Asp Ile Phe Gln
            245 250 255
Met Gln Ala Thr Thr Arg Tyr Pro Gly Ala Tyr Tyr Ile Phe Gln Ile
260 265 270
 Lys Ser Gly Asn Glu Gly Arg Glu Phe Tyr Met Arg Gln Thr Gly Pro
275 280 285
 Ile Ser Ala Thr Leu Val Met Thr Arg Pro Ile Lys Gly Pro Arg Asp 290 295 300
 Ile Gln Leu Asp Leu Glu Met Ile Thr Val Asn Thr Val Ile Asn Phe
 305 310 315 320
 Arg Gly Ser Ser Val Ile Arg Leu Arg Ile Tyr Val Ser Gln Tyr Pro
             325 330
                                                       335 ,
 Phe
```

<210> 187

<211> 152

<212> PRT

<213> mouse

<400> 187

Met Ala Leu Gly Val Leu Ile Ala Val Cys Leu Leu Phe Lys Ala Met
1 5 , 10 15

```
Lys Ala Ala Leu Ser Glu Glu Ala Glu Val Ile Pro Pro Ser Thr Ala .
          20
                            25
Gln Gln Ser Asn Trp Thr Phe Asn Asn Thr Glu Ala Asp Tyr Ile Glu
      35
                        40
Glu Pro Val Ala Leu Lys Phe Ser His Pro Cys Leu Glu Asp His Asn
   50
                    55
                                      60
Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Lys Gln
        70 `
                                 75
Ala Ile Cys Arg Cys Phe Thr Gly Tyr Thr Gly Gln Arg Cys Glu His 85 90 95
     . 85
Leu Thr Leu Thr Ser Tyr Ala Val Asp Ser Tyr Glu Lys Tyr Ile Ala 100 105 110
Ile Gly Ile Gly Val Gly Leu Leu Ile Ser Ala Phe Leu Ala Val Phe
   115 120
                                125
Tyr Cys Tyr Ile Arg Lys Arg Cys Ile Asn Leu Lys Ser Pro Tyr Ile
  130
                   135
                                 140
Ile Cys Ser Gly Gly Ser Pro Leu
     <210> 188
     <211> 118
     <212> PRT
     <213> Rat
     <220>
     <400> 188
Leu Val Pro Gln Phe Gly Thr Arg Ile Arg Tyr ThrAla Tyr Asp Arg
             5
Ala Tyr Asn Arg Ala Ser Cys Lys Phe Ile Val Lys Val Gln Val Arg
       20
                         · 25
Arg Cys Pro Ile Leu Lys Pro Pro Gln His Gly Tyr Leu Thr Cys Ser 35 40 .45
Ser Ala Gly Asp Asn Tyr Gly Ala Ile Cys Glu Tyr His Cys Asp Gly
                                 60
  50 55
Gly Tyr Glu Arg Gln Gly Thr Pro Ser Arg Val Cys Gln Ser Ser Arg
                                  75
              70
Gln Trp Ser Gly Ser Pro Pro Val Cys Thr Pro Met Lys Ile Asn Val
                              90
          85
                                               95
Asn Val Asn Ser Ala Ala Gly Leu Leu Asp Gln Phe Tyr Glu Lys Gln
         100
                  105
Arg Leu Leu Ile Val Ser
      115
     <210> 189
     <211> 299
     <212> PRT
     <213> Human
     <220>
     <400> 189
Met Gly Thr Lys Ala Gln Val Glu Arg Lys Leu Leu Cys Leu Phe Ile
                        10
Leu Ala Ile Leu Cys Ser Leu Ala Leu Gly Ser Val Thr Val His
                   25
```

Ser Ser Glu Pro Glu Val Arg Ile Pro Glu Asn Asn Pro Val Lys Leu

```
35
                       40
Ser Cys Ala Tyr Ser Gly Phe Ser Ser Pro Arg Val Glu Trp Lys Phe
           55
Asp Gln Gly Asp Thr Thr Arg Leu Val Cys Tyr Asn Asn Lys Ile Thr 65 70 75 80
Ala Ser Tyr Glu Asp Arg Val Thr Phe Leu Pro Thr Gly Ile Thr Phe 85 90 95
Lys Ser Val Thr Arg Glu Asp Thr Gly Thr Tyr Thr Cys Met Val Ser
         100
                 105
                                 110
Glu Glu Gly Gly Asn Ser Tyr Gly Glu Val Lys Val Lys Leu Ile Val
115 120 125
Leu Val Pro Pro Ser Lys Pro Thr Val Asn Ile Pro Ser Ser Ala Thr 130 135 140
Ile Gly Asn Arg Ala Val Leu Thr Cys Ser Glu Gln Asp Gly Ser Pro
145 150 155
Pro Ser Glu Tyr Thr Trp Phe Lys Asp Gly Ile Val Met Pro Thr Asn
165 170 175
Pro Lys Ser Thr Arg Ala Phe Ser Asn Ser Ser Tyr Val Leu Asn Pro
180 185 190
Thr Thr Gly Glu Leu Val Phe Asp Pro Leu Ser Ala Ser Asp Thr Gly 195 200 205
Glu Tyr Ser Cys Glu Ala Arg Asn Gly Tyr Gly Thr Pro Met Thr Ser
 210 215
                            220
Asn Ala Val Arg Met Glu Ala Val Glu Arg Asn Val Gly Val Ile Val
225 230 235
Ala Ala Val Leu Val Thr Leu Ile Leu Leu Gly Ile Leu Val Phe Gly 245 250 255
Ile Trp Phe Ala Tyr Ser Arg Gly His Phe Asp Arg Thr Lys Lys Gly
       260 265 270
Thr Ser Ser Lys Lys Val Ile Tyr Ser Gln Pro Ser Ala Arg Ser Glu
    275
                     280
Gly Glu Phe Lys Gln Thr Ser Ser Phe Leu Val
                   295
    <210> 190
    <211> 91
    <212> PRT
    <213> Human
    <400> 190
Gln Pro Thr Val Phe Trp Pro Lys Thr Ser Ala Lys Lys Gly Asn Trp
1 5
                   10 15
Val Leu Arg Leu Gly Leu Ser Asn Pro Asp Arg Pro Ala Arg Gln Asn
        20
                 25
Asn Trp Phe Leu Pro Ala Ser Arg Glu Ile Pro Glu His Ser Ala Leu
                   40
 35
                                    45
Thr Arg Tyr Pro Ala Gln Ile Arg Gly Cys Trp Pro His Arg Leu Thr
         55
                                60 -
Lys Pro Gln Thr Cys Leu Pro Gln Ala Arg Ser Tyr Leu Ser His Glu
               70 75
Val Thr Gln Ala Thr Arg Thr Cys Pro Gly Gly
            85
    <210> 191
     <211> 89
     <212> PRT
```

<213> mouse

<400> 191 Gly Ala Trp Ala Met Leu Tyr Gly Val Ser Met Leu Cys Val Leu Asp 10 . 5 Leu Gly Gln Pro Ser Val Val Glu Glu Pro Gly Cys Gly Pro Gly Lys 20 25 30 Val Gln Asn Gly Ser Gly Asn Asn Thr Arg Cys Cys Ser Leu Tyr Ala · 40 45 Pro Gly Lys Glu Asp Cys Pro Lys Glu Arg Cys Ile Cys Val Thr Pro 55 Glu Tyr His Cys Gly Asp Pro Gln Cys Lys Ile Cys Lys His Tyr Pro 65 70 75 80 Cys Gln Pro Gly Gln Arg Val Glu Val 85

<210> 192 <211> 299 <212> PRT <213> mouse

<220>

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Asn Glu Ile Gly Val Gly Pro Phe Ser Gln Phe Ile Lys Ala Lys Thr
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Arg Pro Leu Pro Pro Ser Pro Pro Arg Leu Glu Cys Ala Ala Ser Gly
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Arg Phe Ile Ser Ile Tyr Arg Gly Pro Ser His Thr Tyr Lys Val Gln
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Glu Ala Gly Glu Gly Pro Tyr Ser Glu Thr Tyr Thr Phe Ser Thr Thr
145 150 155 160
Lys Ser Val Pro Pro Thr Leu Lys Ala Pro Arg Val Thr Gln Leu Glu
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Gly Asn Ser Cys Glu Ile Phe Trp Glu Thr Val Pro Pro Met Arg Gly
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Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp Ser Glu
195 200 205
Tyr Lys Gln Val Tyr Lys Gly Glu Ala Thr Phe Gln Ile Ser Gly 210 215 220
Leu Glm Ser Asn Thr Asp Tyr Arg Phe Arg Val Cys Ala Cys Arg Arg
225 230 235
Cys Val Asp Thr SerGln Glu Leu Ser Gly Ala Phe Ser Pro Ser Ala
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Ala Phe Met Leu Gln Gln Arg Glu Val Met Leu Thr Gly Asp Leu Gly 260 265 270
Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp Glu Gln
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Phe Ala Ala Leu Ile Val Leu Gly Phe Ala Thr Leu Ser Ile Leu Phe
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120

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120

135

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115

125



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     <400> 285
Gly Thr Arg Lys Pro Leu Pro Met Glu Ala His Ser Arg Arg Glu Lys
1 5 10 · 15
Ala Ser Gly Leu Arg Leu Ala Trp His Tyr Glu Cys Ser Gly Val Ser
                            25
          20
Val Trp Trp Met Cys Val Leu Gly Trp Leu Ser Phe Leu Val Phe Leu
                         40
```



Leu Phe Ser Leu Val Cys Ser Phe Pro Ser Pro Ile Asn His Ser His 50 55 60

Met Leu Pro Cys Leu Phe Leu Arg Gly Gly Gly Ser Asn Val 65 70 75

<210> 286 <211> 206 <212> PRT <213> Mouse

<400> 286 Met Leu Pro Pro Ala Ile His Leu Ser Leu Ile Pro Leu Leu Cys Ile 10 Leu Met Arg Asn Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu 20 25 30 Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser 35 40 45 Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Ser Thr Gly 50 55 60 Leu Asp Arg Asn Ser Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser 70 75 Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys 85 90 95 Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn 100 105 110 Trp Ile Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser 120 115 125 Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln 130 135 140 Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val 145 150 150 160 Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Ser 165 170 175 His Asn Phe Glu Ser Val Ser Pro Ala Lys Pro Ala Gln His His Arg 180 185 190 Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Leu Ser 195 200

<210> 287 <211> 169 <212> PRT <213> Mouse

<400> 287

Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly 1 5 10 15 Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg 25 20 . 30 Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly 35 45 40 .Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln 60 50 55 Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu 70 75 Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr 85 90 Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly

```
105
                                                  110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
                        120
      115
                                             125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
                      135
                                          140
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
                 150
                                      155
Gly Glu Met Pro Pro Glu Asp Gly Met
               165
      <210> 288
      <211> 114
      <212> PRT
      <213> Mouse
      <400> 288
Met Ser Val Thr Ile Gly Arg Leu Ala Leu Phe Leu Ile Gly Ile Leu
                                  10
1
Leu Cys Pro Val Ala Pro Ser Leu Thr Arg Ser Trp Pro Gly Pro Asp
           20
                               25
Thr Cys Ser Leu Phe Leu Gln His Ser Leu Ser Leu Ser Leu Arg Leu
                          40
                                              45
Gly Gln Ser Leu Glu Gly Gly Leu Ser Val Cys Phe His Val Cys Ile
   50
                       55
                                         60
His Ala Cys Glu Cys Val Ala Cys Cys Arg Val Leu Trp Asp Pro Lys
                  70
                                      75
Pro Arg Gly Ser Ser Leu Cys Arg Trp Val Leu Gly Ser Ile Thr Cys
                                - 90
               85
Leu Phe Met Tyr Glu Val Gly Gly Trp Thr Gln Gly Gly Leu Ile Val
                               105
            100
Ser Leu
      <210> 289
      <211> 46
      <212> PRT
      <213> Mouse
      <400> 289
Met His Tyr Pro Cys Leu Ala Cys Leu Phe Val Asn Val His Trp Cys
· 1
                5
                                  10
Phe Ala Trp Met Cys Ile Leu Val Lys Met Ser Glu Leu Leu Glu Leu
          20
                              25
                                                  3.0
Glu Leu Glu Thr Met Val Ser Cys Leu Val Asp Val Gly Asn
       35
                           40
   · <210> 290
      <211> 199
      <212> PRT
      <213> Mouse
      <400> 290
Met Val Leu Pro Thr Val Leu Ile Leu Leu Ser Trp Ala Ala Gly
                5
                                  10
Leu Gly Gly Glu Thr Arg Pro Arg Ala Ala Thr Glu Arg Arg Ser Val
           20
                               25
                                                  30
Gly Pro Ser Ala Arg Arg Gly Ala Gly Pro Arg Val Ser Gly Leu Leu
```

```
Gly Phe Cys Gln Leu Ser Gln Leu Ala Ser Ala Asp Pro Glu Arg Arg
                        55
                                           60
Ser Pro Arg Ala Ile Val Pro Arg Ala Pro Arg Pro Arg Ser Arg Arg
                    70
Arg Pro Cys Leu Pro Gly Phe Ser Arg Arg Phe Pro Arg Glu Arg Arg 85 90 95
               85
                                   90
Ser Pro Gly Gln Pro Pro Ser Arg Thr Pro Gln Pro Pro Gln Pro Cys
                              105
           100
Arg Gly Pro Ser Pro Gly Thr Ala Gln Thr Arg Ser Asn Leu Arg Gly
                           120
                                               125
       115
Trp Gln Arg Gly Gly Ser Ile Val Leu Gln Ala Ser Glu Arg Thr Arg
                      135
                                           140
Ala Gly Cys Arg Thr Pro Val Cys Val Ser His Pro Ser Ala Phe Pro 145 150 160
                  150
Pro Pro Arg Ala Leu Phe Gly Val Phe Val Ala Ser Ala Pro Glu Val
                                170
              165
                                            <sub>.</sub> 175
Val Cys Val Cys Val Ser Val Val Leu Ser Val Cys Leu Leu Ser Pro
           180
                               185
                                                   190
Arg Gly Lys Thr Leu Val Asp
       195
      <210> 291
      <211> 568
      <212> PRT
      <213> Rat
      <400> 291
Met Glu Leu Leu Tyr Trp Cys Leu Leu Cys Leu Leu Leu Pro Leu Thr
                                 10
Ser Arg Thr Gln Lys Leu Pro Thr Arg Asp Glu Glu Leu Phe Gln Met
                               25
                                                   30
           20
Gln Ile Arg Asp Lys Ala Leu Phe His Asp Ser Ser Val Ile Pro Asp
                          40
      35
Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr Pro Arg Arg Tyr
                       55
                                           60
Phe Phe Met Val Glu Glu Asp Asn Thr Pro Leu Ser Val Thr Val Thr
                  70
Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu Ser Leu Gln Glu Leu Pro
                                   90
               85 ·
Glu Glu Ser Ser Ala Asp Gly Ser Gly Asp Pro Glu Pro Leu Asp Gln
                               105
                                                   110
           100
Gln Lys Gln Gln Met Thr Asp Val Glu Gly Thr Glu Leu Phe Ser Tyr
115 120 125
        115
                           120
Lys Gly Asn Asp Val Glu Tyr Phe Leu Ser Ser Ser Pro Ser Gly
                                           140
    130
                       135
Leu Tyr Gln Leu Glu Leu Leu Ser Thr Glu Lys Asp Thr His Phe Lys
                                     155
                   150
Val Tyr Ala Thr Thr Thr Pro Glu Ser Asp Gln Pro Tyr Pro Asp Leu
165 170 . 175
                                    170
Pro Tyr Asp Pro Arg Val Asp Val Thr Ser Ile Gly Arg Thr Thr Val
                               185
           180
Thr Leu Ala Trp Lys Gln Ser Pro Thr Ala Ser Met Leu Lys Gln Pro
                           200
                                                205
        195
Ile Glu Tyr Cys Val Val Ile Asn Lys Glu His Asn Phe Lys Ser Leu
                                            220
                        215
Cys Ala Ala Glu Thr Lys Met Ser Ala Asp Asp Ala Phe Met Val Ala
```



```
230
Pro Lys Pro Gly Leu Asp Phe Ser Pro Phe Asp Phe Ala His Phe Gly
                                 250
              245
Phe Pro Thr Asp Asn Leu Gly Lys Asp Arg Ser Phe Leu Ala Lys Pro
                              265
                                                 270
          260
Ser Pro Lys Val Gly Arg His Val Tyr Trp Arg Pro Lys Val Asp Ile
                          280
                                              285
       275
Lys Lys Ile Cys Ile Gly Ser Lys Asn Ile Phe Thr Val Ser Asp Leu
                    295
                                         300
Lys Pro Asn Thr Gln Tyr Tyr Phe Asp Val Phe Met Val Asn Thr Asn
                                      315
                   310
Thr Asn Met Asn Thr Ala Phe Val Gly Ala Phe Ala Arg Thr Lys Glu
              325
                                 330
                                                     335
Glu Ala Lys Gln Lys Thr Val Glu Leu Lys Asp Gly Arg Val Thr Asp 340 345 350
           340
                             345
                                                 350
Val Val Lys Arg Lys Gly Lys Lys Phe Leu Arg Phe Ala Pro Val 355 360 365
       355.
                                             365
Ser Ser His Gln Lys Val Thr Leu Phe Ile His Ser Cys Met Asp Thr
                      375
                                          380
Val Gln Val Gln Val Arg Arg Asp Gly Lys Leu Leu Leu Ser Gln Asn
                   390
                                      395
Val Glu Gly Ile Arg Gln Phe Gln Leu Arg Gly Lys Pro Lys Gly Lys
                                 410
              405
                                                     415
Tyr Leu Ile Arg Leu Lys Gly Asn Lys Lys Gly Ala Ser Met Leu Lys
                              425
           420
                                                 430
Ile Leu Ala Thr Thr Arg Pro Ser Lys His Ala Phe Pro Ser Leu Pro
                          440
                                            445
       435
Asp Asp Thr Arg Ile Lys Ala Phe Asp Lys Leu Arg Thr Cys Ser Ser
                      455
                                         460
    450
Val Thr Val Ala Trp Leu Gly Thr Gln Glu Arg Arg Lys Phe Cys Ile
                  470
                                    475
Tyr Arg Lys Glu Val Gly Gly Asn Tyr Ser Glu Glu Gln Lys Arg Arg
              485
                                  490
Glu Arg Asn Gln Cys Leu Gly Pro Asp Thr Arg Lys Lys Ser Glu Lys
                              505
          500
Val Leu Cys Lys Tyr Phe His Ser Gln Asn Leu Gln Lys Ala Val Thr
                 . 520
                                             525
        515
Thr Glu Thr Ile Arg Asp Leu Gln Pro Gly Lys Ser Tyr Leu Leu Asp
                      535
                                          540
Val Tyr Val Val Gly His Gly Gly His Ser Val Lys Tyr Gln Ser Lys
                                      555
                                                          560
                   550
Leu Val Lys Thr Arg Lys Val Cys
               565
```

<210> 292

<211> 123

<212> PRT

<213> Mouse

<400> 292

Met Leu Thr Glu Pro Ala Gln Leu Phe Val His Lys Lys Asn Gln Pro Pro Ser His Ser Ser Leu Arg Leu His Phe Arg Thr Leu Ala Gly Ala Leu Ala Leu Ser Ser Thr Gln Met Ser Trp Gly Leu Gln Ile Leu Pro Cys Leu Ser Leu Ile Leu Leu Trp Asn Gln Val Pro Gly Leu Glu



```
55
Gly Gln Glu Phe Arg Phe Gly Ser Cys Gln Val Thr Gly Val Val Leu
                  70
                                      75
Pro Glu Leu Trp Glu Ala Phe Trp Thr Val Lys Asn Thr Val Gln Thr
                              90
              85
Gln Asp Asp Ile Thr Ser Ile Arg Leu Leu Lys Pro Gln Val Leu Arg
100 105 110
Asn Val Ser Val Ile Arg Trp Glu Gly Asp Ser
                          120
       115
     <210> 293
     <211> 66
     <212> PRT
     <213> Mouse
     <400> 293
Met Asp Val Trp Ser Gly Leu Pro Leu Glu Thr Leu Trp Ile Tyr Glu
               5
                                 10
Ala Val Leu Pro Trp Leu Leu Met Gly Gln Gly His Ala Trp Val Cys
                             25
        20
                                                30
Gly Pro Ile Ala Leu Trp Val Phe Val Asn Val Pro Gly Leu Cys Tyr
                      40
                                           45
      35 -
His Gln Lys Pro Phe Arg Cys Pro Trp Ser Gly Leu Leu Pro Glu Ala
                      55
                                         60
 50
Leu Cys
65
      <210> 294
      <211> 294
      <212> PRT
      <213> Rat
      <400> 294
Met Thr Val Phe Arg Lys Val Thr Thr Met Ile Ser Trp Met Leu Leu
                               10
Ala Cys Ala Leu Pro Cys Ala Ala Asp Pro Met Leu Gly Ala Phe Ala 20 25 30
       20
                             25
Arg Arg Asp Phe Gln Lys Gly Gly Pro Gln Leu Val Cys Ser Leu Pro
     35
                                           45
                         40
Gly Pro Gln Gly Pro Pro Gly Pro Pro Gly Ala Pro Gly Ser Ser Gly
                     55
                                        60
   50
Met Val Gly Arg Met Gly Phe Pro Gly Lys Asp Gly Gln Asp Gly Gln
                                     75
                 70
Asp Gly Asp Arg Gly Asp Ser Gly Glu Glu Gly Pro Pro Gly Arg Thr 85 90 95
                                 90
              85
Gly Asn Arg Gly Lys Gln Gly Pro Lys Gly Lys Ala Gly Ala Ile Gly
                            105
                                       . 110
          100
Arg Ala Gly Pro Arg Gly Pro Lys Gly Val Ser Gly Thr Pro Gly Lys
115 120 125
His Gly Ile Pro Gly Lys Lys Gly Pro Lys Gly Lys Lys Gly Glu Pro
                    . 135
                                         140
Gly Leu Pro Gly Pro Cys Ser Cys Gly Ser Ser Arg Ala Lys Ser Ala
145 150 155 160
Phe Ser Val Ala Val Thr Lys Ser Tyr Pro Arg Glu Arg Leu Pro Ile
                                170
                                                   175
              165
Lys Phe Asp Lys Ile Leu Met Asn Glu Gly Gly His Tyr Asn Ala Ser
```

185

180



```
Ser Gly Lys Phe Val Cys Ser Val Pro Gly Ile Tyr Tyr Phe Thr Tyr
                         200
       195
Asp Ile Thr Leu Ala Asn Lys His Leu Ala Ile Gly Leu Val His Asn
   210
                     215
                                        220
Gly Gln Tyr Arg Ile Arg Thr Phe Asp Ala Asn Thr Gly Asn His Asp
                 230
                                    235
Val Ala Ser Gly Ser Thr Ile Leu Ala Leu Lys Glu Gly Asp Glu Val
245 250 255
Trp Leu Gln Ile Phe Tyr Ser Glu Gln Asn Gly Leu Phe Tyr Asp Pro
         260
                             265
                                     270
Tyr Trp Thr Asp Ser Leu Phe Thr Gly Phe Leu Ile Tyr Ala Asp Gln
                         280
      275
                                            285
Gly Asp Pro Asn Glu Val
   290
     <210> 295
     <211> 243
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<212> PRT . <213> Rat

<400> 295

Met Arg Pro Leu Leu Ala Leu Leu Leu Leu Gly Leu Ala Ser Gly Ser 5 10 15 Pro Pro Leu Asp Asp Asn Lys Ile Pro Ser Leu Cys Pro Gly Gln Pro 20 25 Gly Leu Pro Gly Thr Pro Gly His His Gly Ser Gln Gly Leu Pro Gly 35 40 45 Arg Asp Gly Arg Asp Gly Arg Asp Gly Ala Pro Gly Ala Pro Gly Glu
50 55 60 50 55 60 Lys Gly Glu Gly Gly Arg Pro Gly Leu Pro Gly Pro Arg Gly Glu Pro 75 70 Gly Pro Arg Gly Glu Ala Gly Pro Val Gly Ala Ile Gly Pro Ala Gly 85 90 Glu Cys Ser Val Pro Pro Arg Ser Ala Phe Ser Ala Lys Arg Ser Glu 100 105 110 Ser Arg Val Pro Pro Pro Ala Asp Thr Pro Leu Pro Phe Asp Arg Val 115 120 . 125 Leu Leu Asn Glu Gln Gly His Tyr Asp Ala Thr Thr Gly Lys Phe Thr 130 135 140 Cys Gln Val Pro Gly Val Tyr Tyr Phe Ala Val His Ala Thr Val Tyr 155 150 Arg Ala Ser Leu Gln Phe Asp Leu Val Lys Asn Gly Gln Ser Ile Ala 170 165 Ser Phe Phe Gln Phe Phe Gly Gly Trp Pro Lys Pro Ala Ser Leu Ser 180 185 190 Gly Gly Ala Met Val Arg Leu Glu Pro Glu Asp Gln Val Trp Val Gln 195 200 205 Val Gly Val Gly Asp Tyr Ile Gly Ile Tyr Ala Ser Ile Lys Thr Asp 215 220 Ser Thr Phe Ser Gly Phe Leu Val Tyr Ser Asp Trp His Ser Ser Pro 235 230 Val Phe Ala

<210> 296 <211> 444 <212> PRT



<213> Rat

<400> 296 Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr 100 105 110 Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu
145 150 155 160 Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser 210 215 Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu Gln His Asp Val Leu Lys Leu Glu Phe Glu Arg His Asp Pro Val Asp Gly Arg Ile Ser Glu Arg Gln Phe Gly Gly Met Leu Leu Ala Tyr Ser Gly Val Gln Ser Lys Lys Leu Thr Ala Met Gln Arg Gln Leu Lys Lys His Phe Lys Asp Gly Lys Gly Leu Thr Phe Gln Glu Val Glu Asn Phe Tyr His Met Ala Gly Ala Ser Leu Asp Lys Val Thr Met Gln Gln Val Ala Arg Thr Val Ala Lys Val Glu Leu Ser Asp His Val Cys Asp Val Val Phe Ala Leu Phe Asp Cys Asp Gly Asn Gly Glu Leu Ser Asn Lys 385 390 395 400 Glu Phe Val Ser Ile Met Lys Glm Arg Leu Met Arg Gly Leu Glu Lys Pro Lys Asp Met Gly Phe Thr Arg Leu Met Gln Ala Met Trp Lys Cys



```
Ala Gln Glu Thr Ala Trp Asp Phe Ala Leu Pro Lys
       435
                         440
     <210> 297
     <211> 65
     <212> PRT
     <213> Human
    <400> 297
Met Thr Met Leu His Leu Ala Val Ile Phe Leu Phe Ser Ala Leu Ser
                                10
Arg Ala Leu Val Gln Cys Ser Ser His Arg Ala Arg Val Val Leu Ser
        20 ·
                             25
                                               30
Trp Ala Asp Tyr Leu Arg Arg Val Ala Pro Thr Ala Leu Ala Thr Ala
            40
      35
                                          45
Leu Asp Val Gly Leu Ser Asn Trp Ser Phe Leu Tyr Val Thr Val Ser
                     55
                                        60
 50
Leu
65
     <210> 298
     <211> 52
     <212> PRT
     <213> Human
     <400> 298
Met Lys Ile Asn Ile Ile Gln Gly Ser Ile Met Ile Leu Leu Ile Cys
                       10
              5
Leu Ser Gln Thr Cys Thr Ser Leu Pro Val Gln Glu Ala Leu Ile Thr
                           25
                                              30
       20
Phe Cys His Leu Tyr Phe Thr Tyr Cys Tyr Ser Gly Asn Ser Asn Lys
      35
                       40
Met Gln Val Leu
   50
     <210> 299
     <211> 41
      <212> PRT
     <213> Human
     <400> 299
Met Pro Cys Val Leu Phe Phe Phe Phe Leu Ser Thr Ser Lys Ser
              5
                                10
 1
Met Ile Tyr Ser Ser Leu Met Leu Gly Leu Tyr Ile Pro Ser Glu Ala
                            25
        20
Cys Val Leu Gly Leu Lys Phe Lys Phe
       35
      <210> 300
      <211> 80
      <212> PRT
      <213> Mouse
      <400> 300
Met Val Trp Gly Thr Leu Leu Gly Arg Val Leu Ala Ala Leu Leu Asn
                                10
                                                   15
Ile Val Pro Thr Glu Ser Ser Tyr Arg Ser Pro Ser Phe Leu Ala Gly
```



```
Phe Arg Phe Cys Cys Ser Pro Trp Ser Gln His Phe Gly Cys Gly Arg
       35
                          40
Leu Thr Ser Cys Leu Pro Pro Cys Val Asp Arg Val Val Lys Thr Tyr
                      55
Ser Ser Pro Pro Cys Leu Ser Val Asn Gly His Asp Val Thr Ile Cys
                  .70
                                       75
    <210> 301
     <211> 82
     <212> PRT
     <213> Mouse
     <400> 301
Met Gly Ser Val Leu Thr Ser Cys Phe Cys Val Gly Gly Ser Ala Glu
                                 10
Ala Trp Asn Trp Leu Pro Ser Ala Ser Ser Leu Phe Pro Cys Cys Ile
         20
                               25
                                                  30
Ala Thr Leu Leu Pro Leu Leu Phe Leu Leu Pro His Leu His Ser Thr
                          40
Leu Ser Arg Val Gln Arg Leu Asn Phe Asn Ile Gly His Leu Gly Val
                      55
                                          60
Tyr Leu Tyr Val Asn Asn Asp Ile Arg Ser Arg Val Thr Pro Leu Leu
                   70
                                      75
Ser Ser
     <210> 302
     <211> 411
      <212> PRT
     <213> Rat
     <400> 302
Met Pro Thr Met Trp Pro Leu Leu His Val Leu Trp Leu Ala Leu Val
                          10
Cys Gly Ser Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala
         20
                              25
Ala Ser Lys Thr Leu Leu Glu Lys Thr Gln Phe Ser Asp Lys Pro Val
       35
                           40
                                              45
Gln Asp Arg Gly Leu Val Val Thr Asp Ile Lys Ala Glu Asp Val Val
                      55
                                          60
Leu Glu His Arg Ser Tyr Cys Ser Ala Arg Ala Arg Glu Arg Asn Phe
                   70
                                      75
Ala Gly Glu Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr
              85
                                 90
Asp Val Ala Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val
           100
                              105
                                                . 110
Trp Leu Gln Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Ile Thr Gly
      115
                          120
                                              125
Leu His Asp Val Asp Gln Gly Trp Met Arg Ala Val Lys Lys His Ala
130 135 140
Lys Gly Val Arg Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr
                 150
                                      155
Asp Asp Phe Arg Ser Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu
              165
                                  170
                                                      175
Ser Lys Thr Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe
           180
                               185
```



```
Val Val Glu Val Trp Ser Gln Leu Leu Ser Gln Lys His Val Gly Leu
      195
                         200
                                           205
Ile His Met Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu
                    215
  210
                                      220
Leu Val Ile Leu Val Ile Pro Pro Ala Val Thr Pro Gly Thr Asp Gln
                 230
                                   235
Leu Gly Met Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Ile Leu
                       ` 250
            245
Asp Gly Phe Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ser Gln Gln Pro
                           265
                                               270
          260
Gly Pro Asn Ala Pro Leu Ser Trp Ile Arg Ala Cys Val Gln Val Leu
      275
                280
Asp Pro Lys Ser Gln Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe 290 295 300
Tyr Gly Met Asp Tyr Ala Ala Ser Lys Asp Ala Arg Glu Pro Val Ile
                310
                                  315
Gly Ala Arg Ala Val Leu Lys Val Ala Leu Pro Leu Ala Val Ser Ser
             325
                               330
                                                   335
Gln Gln Ile Trp Thr Leu Gly Arg Gly Gly Ser Thr Ser Ala Leu Leu
         340
                            345
                                    350
Leu Ala Gly Leu Gly Leu Ala Ser Glu Pro Cys Thr Lys Ser Glu Glu
      355 360 365
Val Pro Lys Lys Ser Leu Leu Asp Thr Val Trp His Trp Gln Gly Glu
 370
                   375
                                       380
Pro Gly Ala Leu Cys Arg Gly Arg Leu His Thr Trp Ile Leu Val Ser
               390
                                  395
Ala Val Pro Gln Ala Cys Thr Cys Leu Phe Gln
      405
```

<210> 303 <211> 617 <212> PRT

<213> Mouse

<400> 303

Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Ser Leu Pro Leu Leu 1 5 10 Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala Cys Pro Cys Leu Arg 20 25 30 Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe 35 40 45 Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys 55 60 Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser 70 75 Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His 90 Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr 100 105 110 Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu 115 120 125 Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu 130 135 140 Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala 150 155 Ser Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser 165 , 170



Ser	Pro	Phe	Asp 180	Thr	Gln	Lys	Ile	Val 185	Ser	Gly	Gly	His	Thr 190	Val	Asp
Leu	Pro	Тут 195	Glu	Phe	Leu	Leu	Pro 200	Cys	Met	Суѕ	Ile	Glu 205	Ala	Ser	Tyr
Leu	Gln 210	Glu	Asp	Thr	Val	Arg 215	Arg	Lys	Lys	Cys	Pro 220	Phe	Gln	Ser	Trp
Pro 225	`Glu	Ala	Tyr	Gly	Ser 230	Asp	Phe	Trp	Gln	Ser 235	Ile	Arg	Phe	Thr	Asp 240
Tyr	Ser	Gln	His	Asn 245	Gln	Met	Val	Met	Ala 250	Leu	Thr	Leu	Arg	Cys 255	Pro
Leu	Lys	Leu	Glu 260	Ala	Ser	Leu	Суѕ	Trp 265	Arg	Gln	Asp	Pro	Leu 270	Thr	Pro
Cys	Glu	Thr 275	Leu	Pro	Asn	Ala	Thr 280	Ala	Gln	Glu	Ser	Glu 285	Gly	Trp	Tyr
Ile	Leu 290	Glu	Asn	Val	Asp	Leu 295	His	Pro	Gln	Leu	Суs 300	Phe	Lys	Phe	Ser
Phe 305	Glu	Asn	Ser	Ser	His 310	Val	Glu	Суѕ	Pro	His 315	Gln	Ser	Gly	Ser	Leu, 320
Pro	Ser	Trp	Thr	Val 325	Ser	Met	Asp	Thr	Gln 330	Ala	Gln	Gln	Leu	Thr 335	Leu
His	Phe	Ser	Ser 340	Arg	Thr	Tyr	Ala	Thr 345	Phe	Ser	Ala	Ala	Trp 350	Ser	Asp
		355					360					Tyr 365			
Gln	Thr 370	Gln	Gly	Ser	Val	Pro 375	Val	Thr	Leu	Asp	Leu 380	Ile	Ile	Pro	Phe
385	_				390					395		Asp			400
Ala	Trp	Lys	His	Val 405	Leu	СЛа	Pro	Asp	Asp 410	Ala	Pro	Tyr	Pro	Thr 415	Gln
			420			•		425				Ь́ь	430		
Leu	His	Ala 435	Ala	Asp	Ser	Glu	Ala 440	Gln	Arg	Arg	Leu	Val 445	Gly	Ala	Leu
	450			_		455					460	Asp			
465		_			470					475		Pro			480
				485					490			Gly		495	
			500					505				Ser	510		
		515					520					Pro 525			
	530					535					540				Arg
545		_			550					555		Asp			560
				565					570			Ala		575	
•			580					585				Leu	590		
		595					600		Asp	Asp	Tyr	Gln 605	Gly	Ser	Thr
Asn	Ser 610	Pro	Сув	Gly	Phe	Ser 615	Cys	Leu							



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Asn His Ile Asn Arg Val Pro Pro Asn Ala Phe Ser Tyr Leu Arg Gln 260 265 270



```
Leu Tyr Arg Leu Asp Met Ser Asn Asn Asn Leu Ser Asn Leu Pro Gln
       275
                        280
Gly Ile Phe Asp Asp Leu Asp Asn Ile Thr Gln Leu Ile Leu Arg Asn
   290
                    295
                                       300
Asn Pro Trp Tyr Cys Gly Cys Lys Met Lys Trp Val Arg Asp Trp Leu 305 310 315 320
                310
                                   315
Gln Ser Leu Pro Val Lys Val Asn Val Arg Gly Leu Met Cys Gln Ala
325 330 335
Pro Glu Lys Val Arg Gly Met Ala Ile Lys Asp Leu Ser Ala Glu Leu 340 345 350
Phe Asp Cys Lys Asp Ser Gly Ile Val Ser Thr Ile Gln Ile Thr Thr
                                  365
                 360
      355
Ala Ile Pro Asn Thr Ala Tyr Pro Ala Gln Gly Gln Trp Pro Ala Pro 370 375 380
Val Thr Lys Gln Pro Asp Ile Lys Asn Pro Lys Leu Ile Lys Asp Gln
         390
                                  395
Arg Thr Thr Gly Ser Pro Ser Arg Lys Thr Ile Leu Ile Thr Val Lys
              405
                               410
                                                 415
Ser Val Thr Pro Asp Thr Ile His Ile Ser Trp Arg Leu Ala Leu Pro
                          425
         420
                                            430
Met Thr Ala Leu Arg Leu Ser Trp Leu Lys Leu Gly His Ser Pro Ala
                        440
                                           445
       435
Phe Gly Ser Ile Thr Glu Thr Ile Val Thr Gly Glu Arg Ser Glu Tyr
 450 455
                                 460
Leu Val Thr Ala Leu Glu Pro Glu Ser Pro Tyr Arg Val Cys Met Val
                                    475
                 470
Pro Met Glu Thr Ser Asn Leu Tyr Leu Phe Asp Glu Thr Pro Val Cys
                                490 .
Ile Glu Thr Gln Thr Ala Pro Leu Arg Met Tyr Asn Pro Thr Thr
                          505 510
          500
Leu Asn Arg Glu Gln Glu Lys Glu Pro Tyr Lys Asn Pro Asn Leu Pro
      515
                         520
                                          525
Leu Ala Ala Ile Ile Gly Gly Ala Val Ala Leu Val Ser Ile Ala Leu
   530
                     535
                                       540
Leu Ala Leu Val Cys Trp Tyr Val His Arg Asn Gly Ser Leu Phe Ser 545 550 555 560
Arg Asn Cys Ala Tyr Ser Lys Gly Arg Arg Arg Lys Asp Asp Tyr Ala
            565 570 575
Glu Ala Gly Thr Lys Lys Asp Asn Ser Ile Leu Glu Ile Arg Glu Thr
                          585
                                              590
          580
Ser Phe Gln Met Leu Pro Ile Ser Asn Glu Pro Ile Ser Lys Glu Glu
      595
                      600
                                          605
Phe Val Ile His Thr Ile Phe Pro Pro Asn Gly Met Asn Leu Tyr Lys
   610 615
                                        620
Asn Asn Leu Ser Glu Ser Ser Ser Asn Arg Ser Tyr Arg Asp Ser Gly
                630
Ile Pro Asp Ser Asp His Ser His Ser
              645
      <210> 306
      <211> 150
      <212> PRT
      <213> Rat
Met Ala Ala Pro Met Asp Arg Thr His Gly Gly Arg Ala Ala Arg Ala
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Leu Arg Arg Ala Leu Ala Leu Ala Ser Leu Ala Gly Leu Leu Ser 20 25 Gly Leu Ala Gly Ala Leu Pro Thr Leu Gly Pro Gly Trp Arg Arg Gln 40 Asn Pro Glu Pro Pro Ala Ser Arg Thr Arg Ser Leu Leu Leu Asp Ala 55 60 Ala Ser Gly Gln Leu Arg Leu Glu Tyr Gly Phe His Pro Asp Ala Val 65. 70 75 Ala Trp Ala Asn Leu Thr Asn Ala Ile Arg Glu Thr Gly Trp Ala Tyr 90 85 Leu Asp Leu Gly Thr Asn Gly Ser Tyr Lys Trp Ile Pro Arg Ala Ala 105 100 Gly Leu Cys Ser Trp Cys Gly Gly Gly Leu Cys Val Arg Gly Ala His 115 120 125 Leu His Ala Leu Asp Glu His Gly Gly Gln Leu Leu Arg Pro Leu Arg 130 135 Val Arg Ser Arg Leu Leu 150 145

<210> 307 <211> 580 <212> PRT <213> Rat

<400> 307 Met Ala Ala Met Pro Leu Gly Leu Ser Leu Leu Leu Val Leu 10 5 Val Gly Gln Gly Cys Cys Gly Arg Val Glu Gly Pro Arg Asp Ser Leu 20 25 Arg Glu Glu Leu Val Ile Thr Pro Leu Pro Ser Gly Asp Val Ala Ala Thr Phe Gln Phe Arg Thr Arg Trp Asp Ser Asp Leu Gln Arg Glu Gly 55 Val Ser His Tyr Arg Leu Phe Pro Lys Ala Leu Gly Gln Leu Ile Ser 70 75 Lys Tyr Ser Leu Arg Glu Leu His Leu Ser Phe Thr Gln Gly Phe Trp 85 90 Arg Thr Arg Tyr Trp Gly Pro Pro Phe Leu Gln Ala Pro Ser Gly Ala 100 105 110 Glu Leu Trp Val Trp Phe Gln Asp Thr Val Thr Asp Val Asp Lys Ser 120 125 115 Trp Lys Glu Leu Ser Asn Val Leu Ser Gly Ile Phe Cys Ala Ser Leu 135 130 140 Asn Phe Ile Asp Ser Thr Asn Thr Val Thr Pro Thr Ala Ser Phe Lys 150 155 Pro Leu Gly Leu Ala Asn Asp Thr Asp His Tyr Phe Leu Arg Tyr Ala 170 165 175 Val Leu Pro Arg Glu Val Val Cys Thr Glu Asn Leu Thr Pro Trp Lys 185 Lys Leu Leu Pro Cys Ser Ser Lys Ala Gly Leu Ser Val Leu Leu Lys 200 205 Ala Asp Arg Leu Phe His Thr Ser Tyr His Ser Gln Ala Val His Ile 215 220

Arg Pro Ile Cys Arg Asn Ala His Cys Thr Ser Ile Ser Trp Glu Leu

Arg Gln Thr Leu Ser Val Val Phe Asp Ala Phe Ile Thr Gly Gln Gly

230

245

. 250 ·

```
Lys Lys Asp Trp Ser Leu Phe Arg Met Phe Ser Arg Thr Leu Thr Glu
                           265
                                            270
Ala Cys Pro Leu Ala Ser Gln Ser Leu Val Tyr Val Asp Ile Thr Gly
       275
                        280
                                          285
Tyr Ser Gln Asp Asn Glu Thr Leu Glu Val Ser Pro Pro Pro Thr Ser
                 295
   290
                                   300
Thr Tyr Gln Asp Val Ile Leu Gly Thr Arg Lys Thr Tyr Ala Val Tyr 305 310 315 320
Asp Leu Phe Asp Thr Ala Met Ile Asn Asn Ser Arg Asn Leu Asn Ile
             325 330
                                        335 .
Gln Leu Lys Trp Lys Arg Pro Pro Asp Asn Glu Ala Leu Pro Val Pro
         340 345 350
Phe Leu His Ala Gln Arg Tyr Val Ser Gly Tyr Gly Leu Gln Lys Gly 355 360 365
           360
                                          365
       355
Glu Leu Ser Thr Leu Leu Tyr Asn Ser His Pro Tyr Arg Ala Phe Pro
                   375
                                    380
   370
Val Leu Leu Asp Ala Val Pro Trp Tyr Leu Arg Leu Tyr Val His
                390
                                   395
Thr Leu Thr Ile Thr Ser Lys Gly Lys Asp Asn Lys Pro Ser Tyr Ile
           405
                              410
His Tyr Gln Pro Ala Gln Asp Arg Gln Gln Pro His Leu Leu Glu Met
         420
                            425
                                            430
Leu Ile Gln Leu Pro Ala Asn Ser Val Thr Lys Val Ser Ile Gln Phe
                       440
Glu Arg Ala Leu Leu Lys Trp Thr Glu Tyr Thr Pro Asp Pro Asn His
                     455
                                      460
Gly Phe Tyr Val Ser Pro Ser Val Leu Ser Ala Leu Val Pro Ser Met 465 470 475 480
         470
                                 475
Val Ala Ala Lys Pro Val Asp Trp Glu Glu Ser Pro Leu Phe Asn Thr
485 490 495
Leu Phe Pro Val Ser Asp Gly Ser Ser Tyr Phe Val Arg Leu Tyr Thr
                 505
                                             510
         500
Glu Pro Leu Leu Val Asn Leu Pro Thr Pro Asp Phe Ser Met Pro Tyr
               520
                                        525
      515
Asn Val Ile Cys Leu Thr Cys Thr Val Val Ala Val Cys Tyr Gly Ser
                    535
                                      540
Phe Tyr Asn Leu Leu Thr Arg Thr Phe His Ile Glu Glu Pro Lys Ser
       550
                         555
545
Gly Gly Leu Ala Lys Arg Leu Ala Asn Leu Ile Arg Arg Ala Arg Gly
            565
Val Pro Pro Leu
      580
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     <211> 283
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     <213> Rat
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Met Thr Ser Gly Pro Gly Gly Pro Ala Ala Ala Thr Gly Gly Lys
                                10
Asp Thr His Gln Trp Tyr Val Cys Asn Arg Glu Lys Leu Cys Glu Ser
                           25
                                             3.0
Leu Gln Ser Val Phe Val Gln Ser Tyr Leu Asp Gln Gly Thr Gln Ile
      35
                        40
                                 45
Phe Leu Asn Asn Ser Ile Glu Lys Ser Gly Trp Leu Phe Ile Gln Leu
    50
                      55
                                       60
```

```
Tyr His Ser Phe Val Ser Ser Val Phe Ser Leu Phe Met Ser Arg Thr
                70
                                  75
Ser Ile Asn Gly Leu Leu Gly Arg Gly Ser Met Phe Val Phe Ser Pro
            85
                              90
                                              95
Asp Gln Phe Gln Arg Leu Leu Lys Ile Asn Pro Asp Trp Lys Thr His
        100
                          105
                                           110 ·
Arg Leu Leu Asp Leu Gly Ala Gly Asp Gly Glu Val Thr Lys Ile Met
                      120
    11.5
                                      125
Ser Pro His Phe Glu Glu Ile Tyr Ala Thr Glu Leu Ser Glu Thr Met
                    135
  130
                                     140
Ile Trp Gln Leu Gln Lys Lys Lys Tyr Arg Val Leu Gly Ile Asn Glu
                        155
     150
Trp Gln Asn Thr Gly Phe Gln Tyr Asp Val Ile Ser Cys Leu Asn Leu
            165 170
Leu Asp Arg Cys Asp Gln Pro Leu Thr Leu Leu Lys Asp Ile Arg Ser
         180
                     185
Val Leu Glu Pro Thr Gln Gly Arg Val Ile Leu Ala Leu Val Leu Pro
     195
                       200
                                       205
Phe His Pro Tyr Val Glu Asn Val Gly Gly Lys Trp Glu Lys Pro Ser
           215
 210
                                 220
Glu Ile Leu Glu Ile Lys Gly Gln Asn Trp Glu Glu Gln Val Asn Ser
               230 235
225
Leu Pro Glu Val Phe Arg Lys Ala Gly Phe Val Ile Glu Ala Phe Thr
                       250
            245
                                               255
Arg Leu Pro Tyr Leu Cys Glu Gly Asp Met Tyr Asn Asp Tyr Tyr Val
                  265
       260
                                            270
Leu Asp Asp. Ala Val Phe Val Leu Arg Pro Val
                        280
      275
     <210> 309
     <211> 37
     <212> PRT
     <213> Rat
     <400> 309
Met Leu Trp Val Leu Leu Ser Leu Thr Pro Leu Leu Ser Pro Leu Ile
1 5 10 15
Phe Phe Pro Val Lys Thr Val Ala Leu Glu Glu Ile Ser Thr Ile Cys
      20
                           25
Arg Ala Asp Val Leu
      35
     <210> 310
     <211> 70
     <212> PRT
     <213> Mouse
     <400> 310
Met Ala Ala Ser Trp Gly Gln Val Leu Ala Leu Val Leu Val Ala Ala
                             10
1
Leu Trp Gly Gly Thr Gln Pro Leu Leu Lys Arg Ala Ser Ser Gly Leu
                          25
      20
Glu Gln Val Arg Glu Arg Thr Trp Ala Trp Gln Leu Leu Gln Glu Ile
                        40
    - 35
Lys Ala Leu Phe Gly Asn Thr Glu Val Arg Leu Ala Leu Thr Asp Glu
   50
                   55
                                     60
Pro Leu Lys Ile Ser Pro
```

```
70
65
     <210> 311
     <211> 58
     <212> PRT
     <213> Human
     <400> 311
Met Leu Leu Ser Ser Leu Val Ser Leu Ala Gly Ser Val Tyr Leu Ala
             5
                              10
Trp Ile Leu Phe Phe Val Leu Tyr Asp Phe Cys Ile Val Cys Ile Thr
                 25
      20
                                            30
Thr Tyr Ala Ile Asn Val Ser Leu Met Trp Leu Ser Phe Arg Lys Val
     35 40
Gln Glu Pro Gln Gly Lys Ala Lys Arg His
  50
                   55
     <210> 312
     <211> 52
     <212> PRT
     <213> Human
     <400> 312
Met Gly Thr Pro Gln Gly Glu Asn Trp Leu Ser Trp Met Phe Glu Lys
             5
1
                              10
                                         15
Leu Val Val Val Met Val Cys Tyr Phe Ile Leu Ser Ile Ile Asn Ser
     20 25
                                    30
Met Ala Gln Ser Tyr Ala Lys Arg Ile Gln Gln Arg Leu Asn Ser Glu
     35
                 · 40
Glu Lys Thr Lys
   50
     <210> 313
<211> 70
     <212> PRT
     <213> Human
    <400> 313
Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly Leu Met Leu Lys
1
                               10
                                               15
Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser Phe Ile Ser Phe
    20
                        25
                                     30
Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met Met Ser Ser Phe
    35
                       40
                                · 45
Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu Gln Asn Pro Gln
Pro Met Thr Pro Pro Trp
     <210> 314
     <211> 58
     <212> PRT
     <213> Mouse
     <400> 314
Met Phe Ile Thr Pro Phe Lys Ala Phe Leu Pro Leu Tyr Leu Leu Thr
              5
                        . 10
```



Glu Leu Ser Leu Ile Asp Ile Thr Ser Cys Asp Asp Leu Pro His Ser 25 Val Leu Pro Gln His Leu Ser Phe Glu Phe Val Leu Trp Ser Met Tyr 35 40 45 Leu Leu Ile Cys Cys Phe Val Ile Ile Phe 55

<210> 315 <211> 229

<212> PRT

<213> Rat

<400> 315

Met Ala Ser Ala Leu Glu Glu Leu Gln Lys Asp Leu Glu Glu Val Lys Val Leu Leu Glu Lys Ser Thr Arg Lys Arg Leu Arg Asp Thr Leu Thr 25 Asn Glu Lys Ser Lys Ile Glu Thr Glu Leu Arg Asn Lys Met Gln Gln 40 Lys Ser Gln Lys Lys Pro Glu Phe Asp Asn Glu Lys Pro Ala Ala Val ` 55 60 Val Ala Pro Leu Thr Thr Gly Tyr Thr Val Lys Ile Ser Asn Tyr Gly 75 65 70 Trp Asp Gln Ser Asp Lys Phe Val Lys Ile Tyr Ile Thr Leu Thr Gly 85 90 95 Val His Gln Val Pro Ala Glu Asn Val Gln Val His Phe Thr Glu Arg 110 105 100 Ser Phe Asp Leu Leu Val Lys Asn Leu Asn Gly Lys Asn Tyr Ser Met 125 115 120 Ile Val Asn Asn Leu Leu Lys Pro Ile Ser Val Glu Ser Ser Ser Lys 130 135 140 Lys Val Lys Thr Asp Thr Val Ile Ile Leu Cys Arg Lys Lys Ala Glu 150 155 145 Asn Thr Arg Trp Asp Tyr Leu Thr Gln Val Glu Lys Glu Cys Lys Glu 170 165 Lys Glu Lys Pro Ser Tyr Asp Thr Glu Ala Asp Pro Ser Glu Gly Leu 180 185 Met Asn Val Leu Lys Lys Ile Tyr Glu Asp Gly Asp Asp Asp Met Lys 200 Arg Thr Ile Asn Lys Ala Trp Val Glu Ser Arg Glu Lys Gln Ala Arg 210 220 Glu Asp Thr Glu Phe

<210> 316 <211> 128 <212> PRT

225

<213> Rat

<400> 316

Arg Ala Glu Phe Gly Thr Ser Gly Glu Met Gly Asn Ala Ala Leu Gly 1 5 10 Ala Glu Leu Gly Val Arg Val Leu Leu Phe Val Ala Phe Leu Ala Thr 20 25 30 Glu Leu Leu Pro Pro Phe Gln Arg Arg Ile Gln Pro Glu Glu Leu Trp 35 40 45 Leu Tyr Arg Asn Pro Tyr Val Glu Ala Glu Tyr Phe Pro Thr Gly Pro



55 60 Met Phe Val Ile Ala Phe Leu Thr Pro Leu Ser Leu Ile Phe Phe Ala 70 75 Lys Phe Leu Arg Lys Ala Asp Ala Thr Asp Ser Lys Gln Ala Cys Leu 90 85 Ala Ala Ser Leu Ala Leu Ala Leu Asn Gly Val Phe Thr Asn Ile Ile
100 105 110 Lys Leu Ile Val Gly Arg Pro Arg Pro Asp Phe Phe Tyr Arg Cys Phe 115 120 125 <210> 317 <211> 75 <212> PRT <213> Rat <400> 317 Ser Ala Gly Val Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile 5 10 Ala Phe Gly Pro Ala Leu Ser Leu Tyr Val Phe Thr Ile Ala Thr Asp 20 25 30 Pro Leu Arg Val Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val 35 40 45 Ser Leu Leu Ser Ser Val Phe Trp Phe Leu Val Arg Val Ile Thr 50 · 55 Asp Asn Arg Asp Gly Pro Val Gln Asn Tyr Leu 70 <210> 318 <211> 43 <212> PRT <213> Human <400> 318 Met Lys Leu Ser Gly Met Phe Leu Leu Ser Leu Ala Leu Phe Cys 10 Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu 20 . 25 Ser Arg Thr Pro Arg Pro Thr Ala Leu Gly Asn 35 40 <210> 319 <211> 86 <212> PRT <213> Mouse <400> 319 Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile 15 5 10 Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser 20 25 Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala 35 40 45 Gly Ala Gln Gly Met Trp Gly Ile Trp Gly His Thr Ile Thr Cys Gly 55 60 Leu Ala Pro Gly Ala Lys Pro Cys Ser Leu Lys Arg Glu Gly Pro Asp 70 80

Leu Leu Ser Phe Pro Pro

85

<210> 320 <211> 60 <212> PRT <213> Mouse

<400> 320

<210> 321 <211> 160 <212> PRT <213> Mouse

<400> 321

Ile Arg His Glu Ala Glu Ala Gly Arg His Gln Pro Glu Gln Leu Ala 10 Ala Asp Ser Arg Thr Glu Thr Val Gly Pro Arg Gln Ser Asn Gly Leu 20 25 30 Thr Gly Pro Gly Leu Pro Thr Trp Gln Leu His Pro Val Leu Phe Pro 35 40 45 Glu Leu Val Leu Trp Val Asn Met Val Pro Cys Phe Leu Leu Ser Leu 55 60 Leu Leu Leu Val Arg Pro Ala Pro Val Val Ala Tyr Ser Val Ser Leu 70 75 Pro Ala Ser Phe Leu Glu Glu Val Ala Gly Ser Gly Glu Ala Glu Gly 85 90 95 90 85 Ser Ser Ala Ser Ser Pro Ser Leu Leu Pro Pro Arg Thr Pro Ala Phe 100 105 110 Ser Pro Thr Pro Gly Arg Thr Gln Pro Thr Ala Pro Val Gly Pro Val 115 120 125 Pro Pro Thr Asn Leu Leu Asp Gly Ile Val Asp Phe Phe Arg Gln Tyr 130 135 140 Val Met Leu Ile Ala Val Val Gly Ser Leu Thr Phe Leu Ile Ser Ser 150 155

<210> 322 <211> 54 <212> PRT <213> Mouse

<400> 322

 Arg Leu Gln Val Asp
 Thr Ser Gly Ser Lys Val Leu Phe Phe Leu Phe Phe
 10
 15

 Phe Phe Phe Phe Leu Cys Val Cys Val Leu Val Cys Cys Cys Phe Gly Phe 25
 30

 Pro Gly Thr His Ser Val Asp Gln Ala Ser Pro Lys Leu Arg Asn Leu 35
 40
 45

 Pro Pro Glu Cys Trp Asp
 45

```
50
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     <211> 280
     <212> PRT
     <213> Mouse
     <400> 323
Leu Asp Ser Arg Ala Cys Arg Ser Thr Leu Val Asp Pro Lys Asn Ser
            5 .
                              10
Ala Arg Glu Asn Ile Arg Glu Tyr Val Arg Trp Met Met Tyr Trp Ile
                           25
         20
Val Phe Ala Ile Phe Met Ala Ala Glu Thr Phe Thr Asp Ile Phe Ile 35 40 45
Ser Trp Ser Gly Pro Arg Ile Gly Arg Pro Trp Gly Trp Glu Gly Pro
                                     60
 50
             55
His His His His Leu Ala Ser Gly Ser His Lys Pro Leu Pro Leu
                                 75
               70
Leu Thr His Arg Phe Pro Phe Tyr Tyr Glu Phe Lys Met Ala Phe Val
             85 90
                                               95
Leu Trp Leu Leu Ser Pro Tyr Thr Lys Gly Ala Ser Leu Leu Tyr Arg
          100
Lys Phe Val His Pro Ser Leu Ser Arg His Glu Lys Glu Ile Asp Ala
              120
                                        125
      115
Cys Ile Val Gln Ala Lys Glu Arg Ser Tyr Glu Thr Met Leu Ser Phe
                   135
                                     140
  130
Gly Lys Arg Ser Leu Asn Ile Ala Ala Ser Ala Ala Val Gln Ala Ala
        150
                                 155
Thr Lys Ser Gln Gly Ala Leu Ala Gly Arg Leu Arg Ser Phe Ser Met
                              170
      165
Gln Asp Leu Arg Ser Ile Pro Asp Thr Pro Val Pro Thr Tyr Gln Asp
                                190
        180
                           185
Pro Leu Tyr Leu Glu Asp Gln Val Pro Arg Arg Arg Pro Pro Ile Gly
     195
                       200
                                         205
Tyr Arg Pro Gly Gly Leu Gln Gly Ser Asp Thr Glu Asp Glu Cys Trp
                  215
                                     220
Ser Asp Asn Glu Ile Val Pro Gln Pro Pro Val Gly Pro Arg Glu Lys
                230 235
Pro Leu Gly Arg Ser Gln Ser Leu Arg Val Val Lys Arg Lys Pro Leu
             245 250
                                                255
Thr Arg Glu Gly Thr Ser Arg Ser Leu Lys Val Arg Thr Pro Lys Lys
         260
                  265
Ala Met Pro Ser Asp Met Asp Ser
       275
                        280
     <210> 324
     <211> 166
     <212> PRT
     <213> Rat
     <400> 324
Ala Leu Arg Arg Val Gly Met Glu Leu Pro Ala Val Asn Leu Lys Val
                             10 . 15
           5
1
```

Ile Leu Leu Val His Trp Leu Leu Thr Thr Trp Gly Cys Leu Ala Phe

40

25 Ser Gly Ser Tyr Ala Trp Gly Asn Phe Thr Ile Leu Ala Leu Gly Val ,

20



```
Trp Ala Val Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu
                   55
                                    60
Gly Gly Leu Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile
                70
                                 75
Phe Tyr Ser Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly
                             90
           85
Met Ala Ile Phe Ser Leu Leu Leu Lys Pro Phe Ser Cys Cys Leu Val
                        105
          100
                                          110
Tyr His Met His Arg Glu Arg Gly Gly Glu Leu Pro Leu Arg Ser Asp
                      120
Phe Phe Gly Pro Ser Gln Glu His Ser Ala Tyr Gln Thr Ile Asp Ser
           135
Ser Asp Ser Pro Ala Asp Pro Leu Ala Ser Leu Glu Asn Lys Gly Gln
       150
                                  155
Ala Ala Pro Arg Gly Tyr
             165
     <210> 325
     <211> 338
     <212> PRT
     <213> Rat
     <400> 325
Ile Arg His Glu Ala Glu Ala Gly Arg His Gln Pro Glu Gln Leu Ala
1 . 5
                             10
Ala Asp Ser Arg Thr Glu Thr Val Gly Pro Arg Gln Ser Asn Gly Leu
      20
                         25
Thr Gly Pro Gly Leu Pro Thr Trp Gln Leu His Pro Val Leu Phe Pro
     35
                       40
                                        45
Glu Leu Val Leu Trp Val Asn Met Val Pro Cys Phe Leu Leu Ser Leu
 50 55
                                    60
Leu Leu Leu Val Arg Pro Ala Pro Val Val Ala Tyr Ser Val Ser Leu
     70
                                 75
Pro Ala Ser Phe Leu Glu Glu Val Ala Gly Ser Gly Glu Ala Glu Gly
    85 90
Ser Ser Ala Ser Ser Pro Ser Leu Leu Pro Pro Arg Thr Pro Ala Phe
        100
                          105
                                           110
Ser Pro Thr Pro Gly Arg Thr Gln Pro Thr Ala Pro Val Gly Pro Val
 115
                     120
                                       125
Pro Pro Thr Asn Leu Leu Asp Gly Ile Val Asp Phe Phe Arg Gln Tyr
  130
                    135
                                     140
Val Met Leu Ile Ala Val Val Gly Ser Leu Thr Phe Leu Ile Met. Phe
                                 155
                150
Ile Val Cys Ala Ala Leu Ile Thr Arg Gln Lys His Lys Ala Thr Ala
                              170
                                               175
             165
Tyr Tyr Pro Ser Ser Phe Pro Glu Lys Lys Tyr Val Asp Gln Arg Asp
         180
                          185 ... 190
Arg Ala Gly Gly Pro His Ala Phe Ser Glu Val Pro Asp Arg Ala Pro
     195
                      200
                                        205
Asp Ser Arg Gln Glu Glu Gly Leu Asp Ser Ser Gln Gln Leu Gln Ala
                   215
                             220
Asp Ile Leu Ala Ala Thr Gln Asn Leu Arg Ser Pro Ala Arg Ala Leu .
225 230 235 240
Pro Gly Ser Gly Glu Gly Thr Lys Gln Val Lys Gly Gly Ser Glu Glu
             245
                             250
                                               255
Glu Glu Glu Lys Glu Glu Glu Val Phe Ser Gly Gln Glu Glu Pro Arg
        260
```



Glu Ala Pro Val Cys Gly Val Thr Glu Glu Lys Pro Glu Val Pro Asp 285

Glu Thr Ala Ser Ala Glu Ala Glu Gly Val Pro Ala Ala Ser Glu Gly 295

Gln Gly Glu Pro Glu Gly Ser Phe Ser Leu Ala Gln Glu Pro Gln Gly 305

Ala Ala Gly Pro Ser Glu Arg Ser Cys Ala Cys Asn Arg Ile Ser Pro 335

Asn Val

<210> 326 <211> 347 <212> PRT

10 Trp Gly Ile Val Leu Glu Thr Val Ala Thr Ala Gly Val Val Thr Ser 25 Val Ala Phe Met Leu Thr Leu Pro Ile Leu Val Cys Lys Val Gln Asp 35 40 Ser Asn Arg Arg Lys Met Leu Pro Thr Gln Phe Leu Phe Leu Gly 50 55 · 60 Val Leu Gly Ile Phe Gly Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp 70 75 Gly Ser Thr Gly Pro Thr Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser 85 90 Ile Cys Phe Ser Cys Leu Leu Ala His Ala Val Ser Leu Thr Lys Leu 100 105 110 Val Arg Gly Arg Lys Pro Leu Ser Leu Leu Val Ile Leu Gly Leu Ala 120 115 125 Val Gly Phe Ser Leu Val Gln Asp Val Ile Ala Ile Glu Tyr Ile Val 135 140 130 Leu Thr Met Asn Arg Thr Asn Val Asn Val Phe Ser Glu Leu Ser Ala 145 150 155 Pro Arg Arg Asn Glu Asp Phe Val Leu Leu Leu Thr Tyr Val Leu Phe 165 170 Leu Met Ala Leu Thr Phe Leu Met Ser Ser Phe Thr Phe Cys Gly Ser 190 180 185 Phe Thr Gly Trp Lys Arg His Gly Ala His Ile Tyr Leu Thr Met Leu 195 200 205 Asp Phe Asp Arg Arg Trp Asp Asp Thr Ile Leu Ser Ser Ala Leu Ala 230 235 ... 240 Ala Asn Gly Trp Val Phe Leu Leu Ala Tyr Val Ser Pro Glu Phe Trp 245 250 Leu Leu Thr Lys Gln Arg Asn Pro Met Asp Tyr Pro Val Glu Asp Ala 260 265 270 260 265 Phe Cys Lys Pro Gln Leu Val Lys Lys Ser Tyr Gly Val Glu Asn Arg 280 . 285 Ala Tyr Ser Gln Glu Glu Ile Thr Gln Gly Phe Glu Glu Thr Gly Asp 295 300 Thr Leu Tyr Ala Pro Tyr Ser Thr His Phe Gln Leu Gln Asn Gln Pro 310 315



```
Pro Gln Lys Glu Phe Ser Ile Pro Arg Ala His Ala Trp Pro Ser Pro
            325
                                330
Tyr Lys Asp Tyr Glu Val Lys Lys Glu Gly Ser
          340
                             345
     <210> 327
     <211> 141
     <212> PRT
     <213> Human
     <400> 327
Lys Asn Ser Lys Cys Leu Leu Phe Trp Cys Arg Lys Ile Val Gly Asn
                                10
Arg Gln Glu Pro Met Trp Glu Phe Asn Phe Lys Phe Lys Gln Ser
          20
                            25
                                               30
Pro Arg Leu Lys Ser Lys Cys Thr Gly Gly Leu Gln Pro Pro Val Gln
      35
                         40
                                            45
Tyr Glu Asp Val His Thr Asn Pro Asp Gln Asp Cys Cys Leu Leu Gln
                   . 55
                                        60
Val Thr Thr Leu Asn Phe Ile Phe Ile Pro Ile Val Met Gly Met Ile
               70
                                   75
Phe Thr Leu Phe Thr Ile Asn Val Ser Thr Asp Met Arg His His Arg
                               90
            85
                                                   95
Val Arg Leu Val Phe Gln Asp Ser Pro Val His Gly Gly Arg Lys Leu
         100
                            105
                                            110
Arg Ser Glu Gln Gly Val Gln Val Ile Leu Asp Gln Cys Thr Ala Phe
    115 120
                                        1.25
Gly Ser Leu Thr Gly Gly Ile Leu Ser Thr His Ser Pro
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                               10
· 1
Cys Cys Cys Leu His Ser Gly Gly Leu Gly Gly Val Pro Leu Pro Pro
     20 .
                             25
                                             30
Phe Pro Pro Gln Ala Gln Arg Gly Glu Gly Pro Gly Lys Trp Met Ser
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    35
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Pro Pro Leu Pro Pro His Pro Val Val Ala Pro Pro Thr Pro Ser Pro
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Ser Arg Gly Cys Val Leu Leu
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Asp Gly Pro Ser Pro Lys Leu Ala Leu Trp Leu Pro Ser Pro Ala Pro
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                                                  ·15
Thr Ala Ala Pro Thr Ala Leu Gly Glu Ala Gly Leu Ala Glu His Ser
           20
                             25
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Gln Arg Asp Asp Arg Trp Leu Leu Val Ala Leu Leu Val Pro Thr Cys 35 40 Val Phe Leu Val Val Leu Leu Ala Leu Gly Ile Val Tyr Cys Thr Arg 50 55 Cys Gly Pro His Ala Pro Asn Lys Arg Ile Thr Asp Cys Tyr Arg Trp 70 75 Val Ile His Ala Gly Ser Lys Ser Pro Thr Glu Pro Met Pro Pro Arg 85 90 Gly Ser Leu Thr Gly Val Gln Thr Cys Arg Thr Ser Val 100 105 <210> 330 <211> 155 <212> PRT <213> Human <400> 330 Ser Val Met Ala Ala Gly Leu Phe Gly Leu Ser Ala Arg Arg Leu Leu Ala Ala Ala Thr Arg Gly Leu Pro Ala Ala Arg Val Arg Trp Glu 20 25 Ser Ser Phe Ser Arg Thr Val Val Ala Pro Ser Ala Val Ala Gly Lys 40 Arg Pro Pro Glu Pro Thr Thr Pro Trp Gln Glu Asp Pro Glu Pro Glu 55 60 Asp Glu Asn Leu Tyr Glu Lys Asn Pro Asp Ser His Gly Tyr Asp Lys 70 75 Asp Pro Val Leu Asp Val Trp Asn Met Arg Leu Val Phe Phe Gly 90 95 Val Ser Ile Ile Leu Val Leu Gly Ser Thr Phe Val Ala Tyr Leu Pro 100 105 110 Asp Tyr Arg Met Lys Glu Trp Ser Arg Arg Glu Ala Glu Arg Leu Val 115 120 125 Lys Tyr Arg Glu Ala Asn Gly Leu Pro Ile Met Glu Ser Asn Cys Phe 135 Asp Pro Ser Lys Ile Gln Leu Pro Glu Asp Glu 145 150 <210> 331 <211> 299 <212> PRT <213> Human <400> 331

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100 .
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Glu Glu Gly Gly Asn Ser Tyr Gly Glu Val Lys Val Lys Leu Ile Val
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Leu Val Pro Pro Ser Lys Pro Thr Val Asn Ile Pro Ser Ser Ala Thr
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Ile Gly Asn Arg Ala Val Leu Thr Cys Ser Glu Gln Asp Gly Ser Pro
145
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Pro Ser Glu Tyr Thr Trp Phè Lys Asp Gly Ile Val Met Pro Thr Asn
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Pro Lys Ser Thr Arg Ala Phe Ser Asn Ser Ser Tyr Val Leu Asn Pro
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                                         190
Thr Thr Gly Glu Leu Val Phe Asp Pro Leu Ser Ala Ser Asp Thr Gly 195 200 205
Glu Tyr Ser Cys Glu Ala Arg Asn Gly Tyr Gly Thr Pro Met Thr Ser 210 215 220 .
Asn Ala Val Arg Met Glu Ala Val Glu Arg Asn Val Gly Val Ile Val
225
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                                     235
Ala Ala Val Leu Val Thr Leu Ile Leu Leu Gly Ile Leu Val Phe Gly
            245 250 255
Ile Trp Phe Ala Tyr Ser Arg Gly His Phe Asp Arg Thr Lys Lys Gly 260 265 270
Thr Ser Ser Lys Lys Val Ile Tyr Ser Gln Pro Ser Ala Arg Ser Glu
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Gly Glu Phe Lys Gln Thr Ser Ser Phe Leu Val
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<400> 332

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195 200 205 Pro Thr Gly Val Pro Cys Asp Pro Ile Ser Gly Leu Cys Leu Cys Pro 215 220 Pro Gly Arg Ala Gly Thr Thr Cys Asp Leu Asp Cys Arg Arg Gly Arg 230 235 Phe Gly Pro Gly Cys Ala Leu Arg Cys Asp Cys Gly Gly Gly Ala Asp 245 250 255 245 250 255 Cys Asp Pro Ile Ser Gly GIn Cys His Cys Val Asp Ser Tyr Thr Gly 260 265 270 Pro Thr Cys Arg Glu Val Pro Thr Gln Leu Ser Ser Ile Arg Pro Ala 275 280 Pro Gln His Ser Ser Ser Lys Ala Met Lys His 295

<210> 333

<211> 109

<212> PRT

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Gly Thr Arg Val Gly Thr Pro Tyr Tyr Met Ser Pro Glu Arg Ile His 10 Glu Asn Gly Tyr Asn Phe Lys Ser Asp Ile Trp Ser Leu Gly Cys Leu . . 20 . 25 30 Leu Tyr Glu Met Ala Ala Leu Gln Ser Pro Phe Tyr Gly Asp Lys Met 35 40 45 Asn Leu Tyr Ser Leu Cys Lys Lys Ile Glu Gln Cys Asp Tyr Pro Pro 55 Leu Pro Ser Asp His Tyr Ser Glu Glu Leu Arg Gln Leu Val Asn Ile 70 75 Cys Ile Asn Pro Asp Pro Glu Lys Arg Pro Asp Ile Ala Tyr Val Tyr 85 90 Asp Val Ala Lys Arg Met His Ala Cys Thr Ala Ser Thr

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<213> Mouse

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	130		Phe			135					140				
Leu 145	Lys	Pro	Ala	Asn	Ile 150	Leu	Leu	qzA	Ala	His 155	Tyr	His	Val	Lys	Ile 160
,			Gly	165					170		•			175	
Leu	Ser	Met	Asp 180	Gly	Leu	Phe	Gly	Thr 185	Ile	Ala	Tyr	Leu	Pro 190	Pro	Glu
Arg	Ile	Arg 195	Glu	Lys	Ser	Arg	Leu 200	Phe	Asp	Thr	Lys	His 205	Asp	Val	Tyr
Ser	Phe 210	Ala	Ile	Val	Ile	Trp 215	Gly	Val	Leu	Thr	Gln 220	Lys	Lys	Pro	Phe
Ala 225	Asp	Glu	Lys	Asn	11e 230	Leu	His	Ile _.	Met	Met 235	Lys	Val	Val	Lys	Gly 240
His	Arg	Pro	Glu	Leu 245	Pro	Pro	Ile	Cys	Arg 250	Pro	Arg	Pro	Arg	Ala 255	Cys
Ala	Ser	Leu	Ile 260	Gly	Leu	Met	Gln	Arg 265	Cys	Trp	His	Ala	Asp 270	Pro	Gln
	_	275	Thr				280					285	,		
Glu	Lуs 290	Pro	Asp	Glu	Glu	Val 295	Lys	Asp	Leu	Ala	His 300	Glu	Pro	Gly	Glu
Lys 305	Ser	Ser	Leu	Glu	Ser 310	Lys	Ser	Glu	Ala	Arg 315	Pro	Glu	Ser	Ser	Arg 320
	_	_		325					330					335	
			Ser 340			-		345				•	350		
		355	Leu				360					365			
	370	_	Lys	_		375	_				380	_			
385		•	Gly		390					395					400
	_		Gly	405					410					415	
			Gly 420					425					430		
		435	Leu				440					445			_
	450		Gly Asn			455					460				
465			Arg		470					475					480
			Val	485					490					495	
_			500 Gln					505					510		_
		515					520					525			
_	530					535					540				Leu
545			Val		550					555					560
			var Ala	565					570					575	
neu	ura	TAT	vra	n.a	TTD	GIII	GLY	114.5	Deu				, _		



585 Ala Lys Gln Pro Gly Val Ser Val Asn Ala Gln Thr Leu Asp Gly Arg 595 600 605 Thr Pro Leu His Leu Ala Ala Gln Arg Gly His Tyr Arg Val Ala Arg 610 615 620 Ile Leu Ile Asp Leu Cys Ser Asp Val Asn Ile Cys Ser Leu Gln Ala 625 630 630 635 640 630 635 Gln Thr Pro Leu His Val Alà Ala Glu Thr Gly His Thr Ser Thr Ala 650 Arg Leu Leu His Arg Gly Ala Gly Lys Glu Ala Leu Thr Ser Glu 660 665 670 Gly Tyr Thr Ala Leu His Leu Ala Ala Gln Asn Gly His Leu Ala Thr 675 685 Val Lys Leu Leu Ile Glu Glu Lys Ala Asp Val Met Ala Arg Gly Pro 695 690 700 Leu Asn Gln Thr Ala Leu His Leu Ala Ala Ala Arg Gly His Ser Glu 710 715 Val Val Glu Glu Leu Val Ser Ala Asp Leu Ile Asp Leu Ser Asp Glu
725 730 735 730 Gln Gly Leu Ser Ala Leu His Leu Ala Ala Gln Gly Arg His Ser Gln 740 745 750 Thr Val Glu Thr Leu Leu Lys His Gly Ala His Ile Asn Leu Gln Ser 755 760 765 Leu Lys Phe Gln Gly Gly Gln Ser Ser Ala Ala Thr Leu Leu Arg Arg 775 770 Ser Lys Thr 785

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20 25 30 Val Asp Val Asn Glu Cys Asp Met Gly Ala Pro Cys Glu Gln Arg Cys 35 40 45 Phe Asn Ser Tyr Gly Thr Phe Leu Cys Arg Cys His Gln Gly Tyr Glu · 55 60 Leu His Arg Asp Gly Phe Ser Cys Ser Asp Ile Asp Glu Cys Ser Tyr 70 75 Ser Ser Tyr Leu Cys Gln Tyr Arg Cys Val Asn Glu Pro Gly Arg Phe 85 90 95 85 90 Ser Cys His Cys Pro Gln Gly Tyr Gln Leu Leu Ala Thr Arg Leu Cys 100 105 110 Gln Asp Ile Asp Glu Cys Glu Ser Gly Ala His Gln Cys Ser Glu Ala 115 120 125 Gln Thr Cys Val Asn Phe His Gly Gly Tyr Arg Cys Val Asp Thr Asn 130 135 140 Arg Cys Val Glu Pro Tyr Ile Gln Val Ser Glu Asn Arg Cys Leu Cys 145 150 155 160 Pro Ala Ser Asn Pro Leu Cys Arg Glu Gln Pro Ser Ser Ile Val His 165 170 Arg Tyr Met Thr Ile Thr Ser Glu Arg Ser Val Pro Ala Asp Val Phe 180 185 190 Gln Ile Gln Ala Thr Ser Val Tyr Pro Gly Ala Tyr Asn Ala Phe Gln . 195 200 205 Ile Arg Ala Gly Asn Ser Gln Gly Asp Phe Tyr Ile Arg Gln Ile Asn 210 215 220 Asn Val Ser Ala Met Leu Val Leu Ala Arg Pro Val Thr Gly Pro Arg 235 230 Glu Tyr Val Leu Asp Leu Glu Met Val Thr Met Asn Ser Leu Met Ser 245 250 Tyr Arg Ala Ser Ser Val Leu Arg Leu Thr Val Phe Val Gly Ala Tyr 265 Thr Phe <210> 337 <211> 316 <212> PRT <213> Mouse <400> 337

His Glu Glu Glu Pro Cys Asn Asn Gly Ser Glu Ile Leu Ala Tyr Asn

Ile Asp Leu Gly Asp Ser Cys Ile Thr Val Gly Asn Thr Thr Thr His 20 25 30

5

15

10



Val Met Lys Asn Leu Leu Pro Glu Thr Thr Tyr Arg Ile Arg Ile Gln . 35 40 Ala Ile Asn Glu Ile Gly Val Gly Pro Phe Ser Gln Phe Ile Lys Ala 50 55 Lys Thr Arg Pro Leu Pro Pro Ser Pro Pro Arg Leu Glu Cys Ala Ala 70 75 Ser Gly Pro Gln Ser Leu Lys Leu Lys Trp Gly Asp Ser Asn Ser Lys 85 90 Thr His Ala Ala Gly Asp Met Val Tyr Thr Leu Gln Leu Glu Asp Arg 100 105 Asn Lys Arg Phe Ile Ser Ile Tyr Arg Gly Pro Ser His Thr Tyr Lys 120 115 125 Val Gln Arg Leu Thr Glu Phe Thr Cys Tyr Ser Phe Arg Ile Gln Ala 135 130 140 Met Ser Glu Ala Gly Glu Gly Pro Tyr Ser Glu Thr Tyr Thr Phe Ser 150 155 Thr Thr Lys Ser Val Pro Pro Thr Leu Lys Ala Pro Arg Val Thr Gln 165 170 . 175 Leu Glu Gly Asn Ser Cys Glu Ile Phe Trp Glu Thr Val Pro Pro Met 185 180 190 Arg Gly Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp 200 195 205 Ser Glu Tyr Lys Gln Val Tyr Lys Gly Glu Glu Ala Thr Phe Gln Ile 210 215 220 Ser Gly Leu Gln Ser Asn Thr Asp Tyr Arg Phe Arg Val Cys Ala Cys . 230 235 Arg Arg Cys Val Asp Thr Ser Gln Glu Leu Ser Gly Ala Phe Ser Pro 245 250 Ser Ala Ala Phe Met Leu Gln Gln Arg Glu Val Met Leu Thr Gly Asp 265 260 Leu Gly Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp 280 Glu Gln Phe Ala Ala Leu Ile Val Leu Gly Phe Ala Thr Leu Ser Ile 290 295 300 Leu Phe Ala Phe Ile Leu Gln Tyr Phe Leu Met Lys 305 310

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<212> PRT

<213> Mouse

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Gln Thr Asn Trp Thr Val Pro Thr Ser Glu Asp Val Thr Lys Val Asn 115 120 125 Leu Gln Val Leu Ile Val Val Asn Arg Thr Ala Ser Lys Ser Ser Val 135 130 140 Lys Met Glu Gln Val Gln Pro Ser Ala Ser Thr Pro Ile Pro Glu Ser 150 155 145 Ser Glu Thr Ser Gln Thr Ile Asn Thr Thr Pro Thr Val Asn Thr Ala 165 ` 170 175 Lys Thr Thr Ala Lys Asp Thr Ala Asn Thr Thr Ala Val Thr Thr Ala 180 185 190 Asn Thr Thr Ala Asn Thr Thr Ala Val Thr Thr Ala Lys Thr Thr Ala 200 205 Lys Ser Leu Ala Ile Arg Thr Leu Gly Ser Pro Leu Ala Gly Ala Leu 210 215 220 His Ile Leu Leu Val Phe Leu Ile Ser Lys Leu Leu Phe 230

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<400> 339

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Ser Asp Gln Glu Thr Leu Arg Ile His Glu Arg Leu Val Ala Gly Ser 280 275 285 Leu Ala Gly Ala Ile Ala Gln Ser Ser Ile Tyr Pro Met Glu Val Leu 290 295 300 Lys Thr Arg Met Ala Leu Arg Lys Thr Gly Gln Tyr Ser Gly Met Leu 310 315 Asp Cys Ala Arg Arg Ile Leu Ala Lys Glu Gly Val Ala Ala Phe Tyr 325 330 325 325 Lys Gly Tyr Ile Pro Asn Met Leu Gly Ile Ile Pro Tyr Ala Gly Ile 340 345 Asp Leu Ala Val Tyr Glu Thr Leu Lys Asn Thr Trp Leu Gln Arg Tyr 355 360 365 Ala Val Asn Ser Ala Asp Pro Gly Val Phe Val Leu Leu Ala Cys Gly 370 375 380 Thr Ile Ser Ser Thr Cys Gly Gln Leu Ala Ser Tyr Pro Leu Ala Leu 385 390 395 Val Arg Thr Arg Met Gln Ala Gln Ala Ser Ile Glu Gly Ala Pro Glu 405 410 415 Val Thr Met Ser Ser Leu Phe Lys Gln Ile Leu Arg Thr Glu Gly Ala 425 420 430 Phe Gly Leu Tyr Arg Gly Leu Ala Pro Asn Phe Met Lys Val Ile Pro 440 435 445 Ala Val Ser Ile Şer Tyr Val Val Tyr Glu Asn Leu Lys Ile Thr Leu 450 455 460 Gly Val Gln Ser Arg 465

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Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Leu Arg Arg Lys Asn
                      55
Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys 65 70 75 80
Val Phe Gly Asn Glu Pro Lys Ala Pro Asp Glu Val Leu Leu Ala Pro
             85
                              90
Arg Thr Glu Thr Ala Glu Ser Thr Pro Ser Trp Gln Val Leu Lys Leu
         100
                           105
                                                 110
Val Phe Cys Ala Ser Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Ile
115 120 125
                                            125
Leu Gln Glu Arg Val Met Thr Gly Ser Tyr Gly Ala Thr Ala Thr Ser
             135
                               140
Pro Gly Glu His Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg
                 150
                                   155
Val Leu Ala Leu Val Val Ala Gly Leu Tyr Cys Val Leu Arg Lys Gln
                               170
             165
Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser
         180
                             185
                                              190
Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser
                         200
                                            205
Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met
                      215
                                         220
Met Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr
               230
                                  235
Leu Thr Ala Gly Leu Ile Ser Ile Gly Val Ser Met Phe Leu Ser 245 250 255
Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu
          260
                           265
                                                270
Val Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp
      275
                        280
                                            285
Gln Asp Ala Leu Phe Ala Tyr Lys Met Ser Ser Val Gln Met Met Phe 290 295 300
Gly Val Asn Leu Phe Ser Cys Leu Phe Thr Val Gly Ser Leu Leu Glu
        310
                                   315
Gln Gly Ala Leu Leu Glu Gly Ala Arg Phe Met Gly Arg His Ser Glu
              325
                                  330
                                                     335
Phe Ala Leu His Ala Leu Leu Leu Ser Ile Cys Ser Ala Phe Gly Gln
          340
                             345
                                                350
Leu Phe Ile Phe Tyr Thr Ile Gly Gln Phe Gly Ala Ala Val Phe Thr 355 360 365
Ile Ile Met Thr Leu Arg Gln Ala Ile Ala Ile Leu Leu Ser Cys Leu
                      375
                                         380
Leu Tyr Gly His Thr Val Thr Val Val Gly Gly Leu Gly Val Ala Val
                390
                                     395
Val Phe Thr Ala Leu Leu Leu Arg Val Tyr Ala Arg Gly Arg Lys Gln
405 410 415
            405
                                410
                                                  415
Arg Gly Lys Lys Ala Val Pro Thr Glu Pro Pro Val Gln Lys Val
                              425
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<211> 51

<212> PRT

<213> Mouse

<400> 342

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Asn Gly Ala Cys Ala Phe His His Glu Leu Lys Gln Ala Ile Cys Arg
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                              25
Cys Phe Thr Gly Tyr Thr Gly Gln Arg Cys Glu His Leu Thr Leu Thr
                       . 40
      35
Ser Tyr Ala
   50
     <210> 343
     <211> 51
     <212> PRT
     <213> Human
     <400> 343
Leu Lys Phe Ser His Leu Cys Leu Glu Asp His Asn Ser Tyr Cys Ile
                                  10
Asn Gly Ala Cys Ala Phe His His Glu Leu Glu Lys Ala Ile Cys Arg
                               25
                                                  30
Cys Phe Thr Gly Tyr Thr Gly Glu Arg Cys Glu His Leu Thr Leu Thr
     35
                           40
Ser Tyr Ala
   50
      <210> 344
     <211> 95
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Ala Ala Ala Leu Leu Leu Leu Leu Leu Ala Leu Tyr Thr Ala Arg Val
                                   10
Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro Lys Ile Arg Tyr
                              25
          20
                                                  30
Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu
     . 35
                          40
                                              45
Glu Lys Met Val Ile Ile Thr Thr Lys Ser Val Ser Arg Tyr Arg Gly
  50
                       55
                                          60
Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile
                 70
                                     75
Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu
         85
                                   90
      <210> 345
      <211> 77
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Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu Glu Lys
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                              25
Met Val Ile Val Thr Thr Lys Ser Met Ser Arg Tyr Arg Gly Gln Glu
       35
                           40
                                              45
His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile Lys Trp
    50
                       55
                                           60
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Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu
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Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro Lys Ile Arg Tyr Ser Asp
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Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu Glu Lys
        20
                          25
Met Val Ile Ile Thr Thr Lys Ser Val Ser Arg Tyr Arg Gly Gln Glu
     35 40 · ·
                                          45
His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile Lys Trp
                    55
                                      60
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Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu
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     <211> 215
     <212> PRT
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Leu Ala Leu His Leu Ser Pro Ser Leu Ser Ala Ser Asp Asn Gly Ser
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                                               30
Cys Val Val Leu Asp Asn Ile Tyr Thr Ser Asp Ile Leu Glu Ile Ser
  35
                        40
                                          45
Thr Met Ala Asn Val Ser Gly Gly Asp Val Thr Tyr Thr Val Thr Val
                   55
                                      60
Pro Val Asn Asp Ser Val Ser Ala Val Ile Leu Lys Ala Val Lys Glu
               70
                                  75
Asp Asp Ser Pro Val Gly Thr Trp Ser Gly Thr Tyr Glu Lys Cys Asn
            85
                             90
Asp Ser Ser Val Tyr Tyr Asn Leu Thr Ser Gln Ser Gln Ser Val Phe
                            105
          100
                                               110
Gln Thr Asn Trp Thr Val Pro Thr Ser Glu Asp Val Thr Lys Val Asn
                        120
                                           125
Leu Gln Val Leu Ile Val Val Asn Arg Thr Ala Ser Lys Ser Ser Val
                      135
                                        140
Lys Met Glu Gln Val Gln Pro Ser Ala Ser Thr Pro Ile Pro Glu Ser
                 150
                                   155 ·
Ser Glu Thr Ser Gln Thr Ile Asn Thr Thr Pro Thr Val Asn Thr Ala
             165
                                170
                                                  175
Lys Thr Thr Ala Lys Asp Thr Ala Asn Thr Thr Ala Val Thr Thr Ala
180 185 190
          180
                            185
                                               190
Asn Thr Thr Ala Asn Thr Thr Ala Val Thr Thr Ala Lys Thr Thr Ala
    195 200
                                            205
Lys Ser Leu Ala Ile Arg Thr
                     215
     <210> 348
     <211> 21
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Pro Gln Phe Leu Asn
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ttetegggea ggegetgegg geteeeegge teeeeggegt eeegggeace egggegggee
                                                                       120
atgegeeegg getagagegt ageeggeegge atgeegetee egetgetget egeegegete
                                                                       180
tgcctcgccg cctccccggc gcccgcgcgc gcctgccagc tgccgtcgga gtggagaccc
                                                                       240
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                                                                       300
ctgcaccccg aggtgcctgg cctctacaac tacctgccgt ggcagtacca agctggagag
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tgtacaaggg tgacaaggac cacattgctg tggaactcta tcgagggcga gttcgagcca
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getatgacae eggeteteae eeggettetg ceatttacag tgtggagaca atcaatgatg
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gaaacttcca cattgtagag ctactgaccc tggattcgag tctttccctc tctgtggatg
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gaggaagccc taaaatcatc accaatttgt caaaacaatc tactctgaat ttcgactctc
                                                                      4620
cactttacgt aggaggtatg cctgggaaaa ataacgtggc ttcgctgcgc caggccctg
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ggcagaacgg caccagcttc catggctgta tccggaacct ttacattaac agtgaactgc
                                                                      4740
aggacttccg gaaagtgcct atgcaaaccg gaattctgcc tggctgtgaa ccatgccaca
                                                                      4800
agaaagtgtg tgcccatggc acatgccagc ccagcagcca atcaggcttc acctgtgaat
                                                                      4860
gtgaggaagg gtggatgggg cccctctgtg accagagaac caatgatccc tgtctcggaa
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acaaatgtgt acatgggacc tgcttgccca tcaacgcctt ctcctacagc tgcaagtgcc
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tggagggcca cggcggggtc ctctgtgatg aagaagaaga tctgtttaac ccctgccagg
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gcagcagtgg attcaccggg gacagctgtg acagagaaat ttcttgtcga ggggaacgga
                                                                      5160
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                                                                      5220
ctcgcttgga gtgcagaggc gggtgtgctg gggggcagtg ctgtggacct ctgagaagca
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                                                                      5340
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                                                                      5460
atatttgaaa tatattgtaa aatacagaac agacttattt ttattatgat aataaagact
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tgtctgcatt tggaaaaaaa ataaaataaa agacacgctt gtactaaaaa aaaaaaaaa
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aaa
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<210> 373
<211> 83
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<212> PRT

<213> Mouse

<400> 373

 Met
 Pro
 Leu
 Pro
 Leu
 Leu
 Leu
 Ala
 Leu
 Cys
 Leu
 Ala
 Ala
 Leu
 Cys
 Leu
 Ala
 Ala
 Ala
 Ala
 Ala
 Leu
 Pro
 Ser
 Glu
 Trp
 Arg
 Pro
 Leu
 Ser

 Ala
 Gly
 Cys
 Arg
 Ala
 Glu
 Leu
 Ala
 Glu
 Thr
 Ile
 Val
 Tyr
 Ala
 Lys
 Val

 Beu
 Ala
 Leu
 His
 Pro
 Glu
 Val
 Pro
 Gly
 Leu
 Tyr
 As
 Tyr
 Leu
 Pro
 Tyr

```
Gln Tyr Gln Ala Gly Glu Gly Gly Leu Phe Tyr Ser Ala Glu Val Glu
                  70
                           75
Met Leu Val
     <210> 374
     <211> 405
     <212> PRT
     <213> Mouse
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Met Pro Pro Leu Leu Leu Pro Ala Ile Tyr Met Leu Leu Phe Phe
1 5
                                10
Arg Val Ser Pro Thr Ile Ser Leu Gln Glu Val His Val Asn Arg Glu
    20
                           25
Thr Met Gly Lys Ile Ala Val Ala Ser Lys Leu Met Trp Cys Ser Ala
  35
                      40
Ala Val Asp Ile Leu Phe Leu Leu Asp Gly Ser His Ser Ile Gly Lys 50 55 60
Gly Ser Phe Glu Arg Ser Lys Arg Phe Ala Ile Ala Ala Cys Asp Ala 65 70 75 80
Leu Asp Ile Ser Pro Gly Arg Val Arg Val Gly Ala Leu Gln Phe Gly
            85
                                90
                                                  95
Ser Thr Pro His Leu Glu Phe Pro Leu Asp Ser Phe Ser Thr Arg Gln
        100 105
                                               110
Glu Val Lys Glu Ser Ile Lys Gly Ile Val Phe Lys Gly Gly Arg Thr
115 120 125
Glu Thr Gly Leu Ala Leu Lys Arg Leu Ser Arg Gly Phe Pro Gly Gly
                    135 140
Arg Asn Gly Ser Val Pro Gln Ile Leu Ile Ile Val Thr Asp Gly Lys
          150
                                  155
Ser Gln Gly Pro Val Ala Leu Pro Ala Lys Gln Leu Arg Glu Arg Gly 165 170 175
Ile Val Val Phe Ala Val Gly Val Arg Phe Pro Arg Trp Asp Glu Leu 180 185 190
Leu Thr Leu Ala Ser Glu Pro Lys Asp Arg His Val Leu Leu Ala Glu
. 195
                      200
                                 205
Gln Val Glu Asp Ala Thr Asn Gly Leu Leu Ser Thr Leu Ser Ser Ser
           215
                             220
Ala Leu Cys Thr Thr Ala Asp Pro Asp Cys Arg Val Glu Pro His Pro 225 230 235 240
Cys Glu Arg Arg Thr Leu Glu Thr Val Arg Glu Leu Ala Gly Asn Ala
             245
                               250 255
Leu Cys Trp Arg Gly Ser Arg Gln Ala Asp Thr Val Leu Ala Leu Pro
         260
                        265
                                  270 .
Cys Pro Phe Tyr Ser Trp Lys Arg Val Phe Gln Thr His Pro Ala Asn 275 280 285
Cys Tyr Arg Thr Ile Cys Pro Gly Pro Cys Asp Ser Gln Pro Cys Gln
290 295 300
                   295
                                      300
Asn Gly Gly Thr Cys Ile Pro Glu Gly Val Asp Arg Tyr His Cys Leu
                310
                                315
Cys Pro Leu Ala Phe Gly Gly Glu Val Asn Cys Ala Pro Lys Leu Ser
             325
                         330
                                                 335
Leu Glu Cys Arg Ile Asp Val Leu Phe Leu Leu Asp Ser Ser Ala Gly 340 345 350
Thr Thr Leu Gly Gly Phe Arg Arg Ala Lys Ala Phe Val Lys Arg Phe
```

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355
                       360
Val Gln Ala Val Leu Arg Glu Asp Ser Arg Ala Arg Val Gly Ile Ala
370 375
                                  380
Ser Tyr Gly Arg Asn Leu Met Val Ala Val Pro Cys Arg Gly Val Pro
385 390
                                 395
Ala Leu Cys Arg Thr
             405
    <210> 375
     <211> 180
     <212> PRT
     <213> Mouse
     <400> 375
Met Glu Leu Ser Asp Val Thr Leu Ile Glu Gly Val Gly Asn Glu Val
           5
                    10
                                             15
Met Val Val Ala Gly Val Val Ala Leu Thr Leu Ala Leu Val Leu Ala
       20
                      25
                                          3.0
Trp Leu Ser Thr Tyr Val Ala Asp Ser Gly Asn Asn Gln Leu Leu Gly
                     40
                                       45
Thr Ile Val Ser Ala Gly Asp Thr Ser Val Leu His Leu Gly His Val 50 55 60
Asp Gln Leu Val Asn Gln Gly Thr Pro Glu Pro Thr Glu His Pro His
      · 70
                                75
Pro Ser Gly Gly Asn Asp Asp Lys Ala Glu Glu Thr Ser Asp Ser Gly
             85
                    90
Gly Asp Ala Thr Gly Glu Pro Gly Ala Arg Gly Glu Met Glu Pro Ser
100 105 110
Leu Glu His Leu Leu Asp Ile Gln Gly Leu Pro Lys Arg Gln Ala Gly
 115 120
                               125
Leu Gly Ser Ser Arg Pro Glu Ala Pro Leu Gly Leu Asp Asp Gly Ser
130 135 140
Cys Leu Ser Pro Ser Pro Ser Leu Ile Asn Val Arg Leu Lys Phe Leu
145 150 155
                                                160
Asn Asp Thr Glu Glu Leu Ala Val Ala Arg Pro Glu Asp Thr Val Gly
   165
                             170
Thr Leu Lys Arg
. 180
    <210> 376
     <211> 68
     <212> PRT
     <213> Mouse
    <400> 376
Met Cys Leu Pro Val Thr Val Trp Cys His Trp Ala Leu Trp Val Aļa
                             10
His Leu Pro Leu Ile Pro Ser Val Gly Lys Ser Gln Cys Thr Gln Met 20 25 30
Trp His Cys Cys Met Pro Trp Val Cys Val Gly Asp Cys Leu Cys Leu
   . 35 40
                                     45
Ser Asp Pro Leu Trp Leu Cys Leu Leu Lys Glu Thr Glu Thr Pro Cys
                    55
 50
Gly Phe Leu Ser
```

<210> 377

<211> 107 <212> PRT <213> Rat <400> 377 Met Pro Phe Arg Leu Leu Ile Pro Leu Gly Leu Val Cys Val Leu Leu 1 5 10 15 Pro Leu His His Gly Ala Pro Gly Pro Glu Gly Thr Ala Pro Asp Pro 20 25 Ala His Tyr Arg Glu Arg Val Lys Ala Met Phe Tyr His Ala Tyr Asp 35 40 45 Ser Tyr Leu Glu Asn Ala Phe Pro Tyr Asp Glu Leu Arg Pro Leu Thr 55 60 Cys Asp Gly His Asp Thr Trp Gly Ser Phe Ser Leu Thr Leu Ile Asp 65 70 75 80 Ala Leu Asp Thr Leu Leu Ile Leu Gly Asn Thr Ser Glu Phe Gln Arg 85 90 Val Val Glu Val Leu Gln Asp Lys Arg Gly Leu 100 105 <210> 378 <211> 95 <212> PRT <213> Rat <400> 378 Met Trp Phe Leu Pro Cys Ser Val Pro Leu Val Ile Ser Ser Cys His 5 . 10 Ser Gln Ala Ser Pro His Trp Pro Tyr Gly Ile Ile Ser Gly Gly Gln 20 25 30 Glu Gly Leu Cys Arg Leu Trp Thr Ala Thr Cys His Ser Arg Gly Glu 35 40 45 Ser Glu Val Ser Arg Ser Ser Arg Lys Glu Asp Pro Arg Ile Pro Gln 55 60 Gly Ser Leu Ser Gly Asn Val Asp Phe Trp Arg Val Cys Pro Pro Cys 65 70 75 80 70 75 Ala His Thr Ser Met Asp Arg Thr Leu Gly Leu Leu Ser Cys Cys 90 <210> 379 <211> 138 <212> PRT <213> Mouse <400> 379

 Met
 Asp
 Leu
 Asp
 Val
 Val
 Asn
 Met
 Phe
 Val
 Ile
 Ala
 Gly
 Thr
 Leu

 1
 1
 5
 10
 10
 15
 15
 15
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```
Asn Leu His Leu Val Cys Val Asp Met Pro Gly His Glu Gly Thr Thr
                           105
         100
                                             110.
Arg Ser Ser Leu Asp Asp Leu Ser Ile Val Gly Gln Val Lys Arg Ile
     115
                120
                                          125
His Gln Phe Val Glu Cys Leu Lys Leu Asn
                    135
     <210> 380
     <211> 81
     <212> PRT
     <213> Rat
     <400> 380
Met Ala Ser Ser Ser Asn Trp Leu Ser Gly Val Asn Val Val Leu Val
           5
                          10
Met Ala Tyr Gly Ser Leu Val Phe Val Leu Leu Phe Ile Phe Val Lys
         20
                           25
                                            30
Arg Gln Ile Met Arg Phe Ala Met Lys Ser Arg Arg Gly Pro His Val
                       40
                                45
Pro Val Gly His Asn Ala Pro Lys Asp Leu Lys Glu Glu Ile Asp Ile
                   55
                                      60
Arg Leu Ser Arg Val Gln Asp Ile Lys Tyr Glu Pro Gln Leu Leu Ala
                 70
Asp
     <210> 381
     <211> 257
     <212> PRT
     <213> Mouse
    <400> 381
Met Arg Ser Gly Ala Leu Trp Pro Leu Leu Trp Gly Ala Leu Val Trp
             5
                              10
Thr Val Gly Ser Val Gly Ala Val Met Gly Ser Glu Asp Ser Val Pro
    20
                           25
                                            30
Gly Gly Val Cys Trp Leu Gln Gln Gly Arg Glu Ala Thr Cys Ser Leu
     35
                       40
                                          4.5
Val Leu Lys Thr Arg Val Ser Arg Glu Glu Cys Cys Ala Ser Gly Asn
 50 55
                                     60
Ile Asn Thr Ala Trp Ser Asn Phe Thr His Pro Gly Asn Lys Ile Ser
                70
                                75
Leu Leu Gly Phe Leu Gly Leu Val His Cys Leu Pro Cys Lys Asp Ser
            85
                             90
Cys Asp Gly Val Glu Cys Gly Pro Gly Lys Ala Cys Arg Met Leu Gly
         100
                         105
                                             110
Gly Arg Pro Thr Leu Arg Ser Cys Val Pro Asn Cys Glu Gly Leu Pro
      115
               120
                                 125
Ala Gly Phe Gln Val Cys Gly Ser Asp Gly Ala Thr Tyr Arg Asp Glu
130 135 140
   130
                   135
                                     140
Cys Glu Leu Arg Thr Ala Arg Cys Arg Gly His Pro Asp Leu Arg Val
145
             150
                                  155
Met Tyr Arg Gly Arg Cys Gln Lys Ser Cys Ala Gln Val Val Cys Pro
           165 170 175
Arg Pro Gln Ser Cys Leu Val Asp Gln Thr Gly Ser Ala His Cys Val 180 185 190
```

Val Cys Arg Ala Ala Pro Cys Pro Val Pro Ser Asn Pro Gly Gln Glu

200

195

```
Leu Cys Gly Asn Asn Asn Val Thr Tyr Ile Ser Ser Cys His Leu Arg
 210
         215
                                        220
Gln Ala Thr Cys Phe Leu Gly Arg Ser Ile Gly Val Arg His Pro Gly
225 230
                                   235 240
Ile Cys Thr Gly Gly Pro Lys Val Pro Ala Glu Glu Glu Glu Asn Phe
             245
                           250
     <210> 382
     <211> 285
     <212> PRT -
     <213> Rat
     <400> 382
Met Ile Ser Trp Met Leu Leu Ala Cys Ala Leu Pro Cys Ala Ala Asp
               5
                                 10
Pro Met Leu Gly Ala Phe Ala Arg Arg Asp Phe Gln Lys Gly Gly Pro 20 25 30
Gln Leu Val Cys Ser Leu Pro Gly Pro Gln Gly Pro Pro Gly Pro Pro 35 40 45
Gly Ala Pro Gly Ser Ser Gly Met Val Gly Arg Met Gly Phe Pro Gly
 50 55
                                        60
Lys Asp Gly Gln Asp Gly Gln Asp Gly Asp Gly Asp Ser Gly Glu 65 70 75 80
                                    75
Glu Gly Pro Pro Gly Arg Thr Gly Asn Arg Gly Lys Gln Gly Pro Lys
85 90 95
             85
                             90
Gly Lys Ala Gly Ala Ile Gly Arg Ala Gly Pro Arg Gly Pro Lys Gly
                            105
                                     110
Val Ser Gly Thr Pro Gly Lys His Gly Ile Pro Gly Lys Lys Gly Pro
      115
                        120
                                           125
Lys Gly Lys Lys Gly Glu Pro Gly Leu Pro Gly Pro Cys Ser Cys Gly 130 135 140
Ser Ser Arg Ala Lys Ser Ala Phe Ser Val Ser Val Thr Lys Ser Tyr 145 150 150 160
Pro Arg Glu Arg Leu Pro Ile Lys Phe Asp Lys Ile Leu Met Asn Glu . 165 170 175
Gly Gly His Tyr Asn Ala Ser Ser Gly Lys Phe Val Cys Ser Val Pro
       180 185 190
Gly Ile Tyr Tyr Phe Thr Tyr Asp Ile Thr Leu Ala Asn Lys His Leu 195 200 205
Ala Ile Gly Leu Val His Asn Gly Gln Tyr Arg Ile Arg Thr Phe Asp
                    215
                              220
Ala Asn Thr Gly Asn His Asp Val Ala Ser Gly Ser Thr Ile Leu Ala
               230
                                 235
Leu Lys Glu Gly Asp Glu Val. Trp Leu Gln Ile Phe Tyr Ser Glu Gln
             245
                       250
                                                  255
Asn Gly Leu Phe Tyr Asp Pro Tyr Trp Thr Asp Ser Leu Phe Thr Gly 260 265 270
Phe Leu Ile Tyr Ala Asp Gln Gly Asp Pro Asn Glu Val
      275
                         280
                                        285
     <210> 383
     <211> 183
     <212> PRT
     <213> Rat
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Met Lys Leu Cys Leu Val Ala Val Val Gly Cys Leu Leu Val Pro
                                 10
Pro Ala Gln Ala Asn Lys Ser Ser Glu Asp Ile Arg Cys Lys Cys Ile
       20
                            25
Cys Pro Pro Tyr Arg Asn Ile Ser Gly His Ile Tyr Asn Gln Asn Val
     35 ` 40
                                          45
Ser Gln Lys Asp Cys Asn Cys Leu His Val Val Glu Pro Met Pro Val
                  55
                                     60
Pro Gly His Asp Val Glu Ala Tyr Cys Leu Leu Cys Glu Cys Arg Tyr
      70
Glu Glu Arg Ser Thr Thr Thr Ile Lys Val Ile Ile Val Ile Tyr Leu
85 90 95
Ser Val Val Gly Ala Leu Leu Leu Tyr Met Ala Phe Leu Met Leu Val
         100 105
                                              110
Asp Pro Leu Ile Arg Lys Pro Asp Ala Tyr Thr Glu Gln Leu His Asn
                 120
      115
                                         125
Glu Glu Glu Asn Glu Asp Ala Arg Ser Met Ala Ala Ala Ala Ala Ser
130 135 140
                                140
Ile Gly Gly Pro Arg Ala Asn Thr Val Leu Glu Arg Val Glu Gly Ala
145 150 155
Gln Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Thr Val Phe
165 170 175
                               170
Asp Arg His Lys Met Leu Ser
         180
     <210> 384
     <211> 292
     <212> PRT
     <213> Mouse
     <400> 384
Cys Gln Leu Pro Leu Arg Val Leu Ile Ile Ser Asn Asn Lys Leu Gly
1 5 10 15
Ala Leu Pro Pro Asp Ile Ser Thr Leu Gly Ser Leu Arg Gln Leu Asp
                            25
Val Ser Ser Asn Glu Leu Gln Ser Leu Pro Val Glu Leu Cys Ser Leu
     35
                        40
Arg Ser Leu Arg Asp Leu Asn Val Arg Arg Asn Gln Leu Ser Thr Leu 50 55 60
                                     60
Pro Asp Glu Leu Gly Asp Leu Pro Leu Val Arg Leu Asp Phe Ser Cys 65 70 75 80
Asn Arg Ile Ser Arg Ile Pro Val Ser Phe Cys Arg Leu Arg His Leu
            85
                               90
                                                  95
Gln Val Val Leu Leu Asp Ser Asn Pro Leu Gln Ser Pro Pro Ala Gln
                           105 ., 110
         100
Ile Cys Leu Lys Gly Lys Leu His Ile Phe Lys Tyr Leu Thr Met Glu
115 120 125
Ala Gly Arg Arg Gly Ala Ala Leu Gly Asp Leu Val Pro Ser Arg Pro
  130
                    135
                                 140
Pro Ser Phe Ser Pro Cys Pro Ala Glu Asp Leu Phe Pro Gly Arg Arg
               150
                                   155
Tyr Asp Gly Gly Leu Asp Ser Gly Phe His Ser Val Asp Ser Gly Ser
             165
                       170
                                                  175
Lys Arg Trp Ser Gly Asn Glu Ser Thr Asp Asp Phe Ser Glu Leu Ser
```

190

185

180

```
Phe Arg Ile Ser Glu Leu Ala Arg Asp Pro Arg Gly Pro Arg Gln Pro
      195
                        200
Arg Glu Asp Gly Ala Gly Asp Gly Asp Leu Glu Gln Ile Asp Phe Ile
 210
                    215
                                      220
Asp Ser His Val Pro Gly Glu Asp Glu Asp Arg Ser Ala Ala Glu Glu 225 230 230 235
225
                230
                          235
Gln Leu Pro Ser Glu Leu Ser Leu Val Ala Gly Asp Val Glu Lys Pro
 245 ` 250
Ser Ser Ser Arg Arg Glu Glu Pro Ala Gly Glu Glu Arg Arg Pro 260 265 270
                                             270
Asp Thr Leu Gln Leu Trp Gln Glu Arg Glu Arg Lys Gln Gln Gln
              280
                                          285
Ser Gly Gly Trp
   290
     <210> 385
     <211> 164
     <212> PRT
     <213> Mouse
     <400> 385
Ser Arg Gln Leu Arg Ala Pro Arg Phe Asp Pro Arg Ala Gly Phe His
1 5
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Ala Glu Gly Lys Asp Arg Gly Pro Ser Val Pro Gln Gly Leu Leu Lys
         20
                          25
                                             30
Ala Ala Arg Ser Ser Gly Gln Leu Asn Leu Ala Gly Arg Asn Leu Gly
     35
                       40
Glu Val Pro Gln Cys Val Trp Arg Ile Asn Val Asp Ile Pro Glu Glu 50 55 60
Ala Asn Gln Asn Leu Ser Phe Ser Ser Thr Glu Arg Trp Trp Asp Gln
65 70
                                 75
Thr Asp Leu Thr Lys Leu Ile Ile Ser Ser Asn Lys Leu Gln Ser Leu
           85
                          9.0
Ser Asp Asp Leu Arg Leu Leu Pro Ala Leu Thr Val Leu Asp Ile His 100 105 110
Asp Asn Gln Leu Thr Ser Leu Pro Ser Ala Ile Arg Glu Leu Asp Asn
 115 120 125
Leu Gln Lys Leu Asn Val Ser His Asn Lys Leu Lys Ile Leu Pro Glu
        · 135
                                   140
Glu Ile Thr Ser Leu Lys Asn Leu Arg Thr Leu His Leu Gln His Asn
                150
                                155
                                                    160
Glu Leu Thr Cys
    <210> 386
     <211> 71
     <212> PRT
     <213> Mouse
    <400> 386
Ser Leu Ser Ile Leu Pro Ala Val Arg Val Ser Pro Arg Pro Thr Tyr
                              10
Pro Ser Thr Ala Ser Ser Met Ala Ala Phe Leu Val Thr Gly Phe Phe
    20
                           25
Phe Ser Leu Phe Val Val Leu Gly Met Glu Pro Arg Ala Leu Phe Arg
     35
                      40
                                         45
Pro Asp Lys Ala Leu Pro Leu Ser Cys Ala Lys Pro Thr Ser Leu Cys
```

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Val Gln Ser Ser Phe Leu Gly
     <210> 387
     <211> 126
     <212> PRT
     <213> Mouse
     <400> 387
Glu Tyr Glu Ala Arg Val Leu Glu Lys Ser Leu Arg Lys Glu Ser Arg
                                 10
Asn Lys Glu Thr Asp Lys Val Lys Leu Thr Trp Arg Asp Arg Phe Pro
                            25
Ala Tyr Phe Thr Asn Leu Val Ser Ile Ile Phe Met Ile Ala Val Thr
       35
               40
Phe Ala Ile Val Leu Gly Val Ile Ile Tyr Arg Ile Ser Thr Ala Ala
                  _____55
                                     60
Ala Leu Ala Met Asn Ser Ser Pro Ser Val Arg Ser Asn Ile Arg Val
              70
                                 75
Thr Val Thr Ala Thr Ala Val Ile Ile Asn Leu Val Val Ile Ile Leu
85 90 95
Leu Asp Glu Val Tyr Gly Cys Ile Ala Arg Trp Leu Thr Lys Ile Gly
       100 105 110
Glu Cys His Val Gln Asp Ser Ile Gly Ser Met Gly Leu Gly
                      120
     <210> 388
     <211> 84
     <212> PRT
     <213> Rat
     <400> 388
Ala Ala Glu Asn Glu Met Pro Val Ala Val Gly Pro Tyr Gly Gln Ser
                            10
Gln Pro Ser Cys Phe Asp Arg Val Lys Met Gly Phe Val Met Gly Cys 20 25 30
Ala Val Gly Met Ala Ala Gly Ala Leu Phe Gly Thr Phe Ser Cys Leu
      35 . 40
Arg Ile Gly Met Arg Gly Arg Glu Leu Met Gly Gly Ile Gly Lys Thr
                     55
                                       60
Met Met Gln Ser Gly Gly Thr Phe Gly Thr Phe Met Ala Ile Gly Met
                  70
Gly Ile Arg Cys
     <210> 389
     <211> 284
     <212> PRT
     <213> Rat
     <400> 389
Gly Gly Ser Ser Val Ser His Val Leu Arg Gly Ser Gly Gln Glu Arg
               5
                                10
Ser Pro Pro Pro Ala Ser Met Gln Pro Pro Trp Gly Leu Ala Leu Pro
                            25
Leu Leu Pro Trp Val Ala Gly Gly Val Gly Thr Ser Pro Arg Asp
```

```
Tyr Trp Leu Pro Ala Leu Ala His Gln Pro Gly Val Cys His Tyr Gly
                   55
  50
                                               60
Thr Lys Thr Ala Cys Cys Tyr Gly Trp Lys Arg Asn Ser Lys Gly Val 65 70 75 80
Cys Glu Ala Val Cys Glu Pro Arg Cys Lys Phe Gly Glu Cys Val Gly
85 90 95
Pro Asn Lys Cys Arg Cys Phè Pro Gly Tyr Thr Gly Lys. Thr Cys Ser 100 105 110
Gln Asp Val Asn Glu Cys Ala Phe Lys Pro Arg Pro Cys Gln His Arg
115 120 125
Cys Val Asn Thr His Gly Ser Tyr Lys Cys Phe Cys Leu Ser Gly His
  130 135
                                    140
Met Leu Leu Pro Asp Ala Thr Cys Ser Asn Ser Arg Thr Cys Ala Arg
145 150 155 160
Ile Asn Cys Gln Tyr Ser Cys Glu Asp Thr Ala Glu Gly Pro. Arg Cys
165 170 175
Val Cys Pro Ser Ser Gly Leu Arg Leu Gly Pro Asn Gly Arg Val Cys
180 185 190
Leu Asp Ile Asp Glu Cys Ala Ser Ser Lys Ala Val Cys Pro Ser Asn 195 200 205
Arg Arg Cys Val Asn Thr Phe Gly Ser Tyr Tyr Cys Lys Cys His Ile 210 \phantom{\bigg|}215\phantom{\bigg|}220\phantom{\bigg|}
Gly Phe Glu Leu Lys Tyr Ile Ser Arg Arg Tyr Asp Cys Val Asp Ile 225 230 235 240
Asn Glu Cys Thr Leu Asn Thr Arg Thr Cys Ser Pro His Ala Asn Cys
          245
                           250 255
Leu Asn Thr Gln Gly Ser Phe Lys Cys Lys Cys Lys Gln Gly Tyr Arg 260 265 270
Gly Asn Gly Leu Gln Cys Ser Val Ile Pro Glu His
       275
                              280.
      <210> 390
      <211> 85
      <212> PRT
      <213> Rat
      <400> 390
Gly Ala Pro Met Tyr Phe Ser Glu Gly Arg Glu Arg Gly Lys Val Tyr
1 5 10 15
                                      10
Val Tyr Asn Leu Arg Gln Asn Arg Phe Val Phe Asn Gly Thr Leu Lys 20 25 30
Asp Ser His Ser Tyr Gln Asn Ala Arg Phe Gly Ser Cys Ile Ala Ser \cdot 35 40 45
Val Gln Asp Leu Asn Gln Asp Ser Tyr Asn Asp Val Val Gly Ala
                        55
                                              60
Pro Gln Glu Asp Ser His Arg Gly Ala Ile Tyr Ile Phe His Gly Phe
Gln Thr Asn Ile Leu
               85
      <210> 391
      <211> 158
      <212> PRT
      <213> Rat
      <400> 391
```

```
Phe Gln Thr Asn Ile Leu Lys Lys Pro Val Gln Arg Ile Ser Ala Ser
               5
                                 10
Glu Leu Ala Pro Gly Leu Gln His Phe Gly Cys Ser Ile His Gly Gln
          20
                             25
Leu Asp Leu Asn Glu Asp Gly Leu Val Asp Leu Ala Val Gly Ala Leu
      35
                         40
                                            45
Gly Asn Ala Val Val Leu Trp Ala Arg Pro Val Val Gln Ile Asn Ala
                   55`
                                      60
Ser Leu His Phe Glu Pro Ser Lys Ile Asn Ile Phe His Lys Asp Cys
                70
                                   75
Lys Arg Asn Gly Arg Asp Ala Thr Cys Leu Ala Ala Phe Leu Cys Phe
             85
                                90
Gly Pro Ile Phe Leu Ala Pro His Phe His Thr Ala Thr Val Gly Ile
          100
                             105
                                      . 110
Arg Tyr Asn Ala Thr Met Asp Glu Arg Arg Tyr Met Pro Arg Ala His
      115
                         120
                                       125
Leu Asp Glu Gly Ala Asp Gln Phe Thr Asn Arg Ala Val Leu Leu Ser
  130
                     135
                                        140
Ser Gly Gln Glu His Cys Gln Arg Ile Asn Phe His Val Leu
                  150
    <210> 392
     <211> 124
     <212> PRT
     <213> Mouse
     <400> 392
Ala Ala Glu Gln Glu Ala Ser Ser Arg Arg Arg Gly Gly Ala Gly
1
               5
                                 10
Pro Ala Leu Phe Ser Ser Gly Ser Leu Arg Ser Glu Pro Gln Pro Arg
    20
                             25
                                                30
Leu Pro Gln Ala Arg Ser Arg Pro Arg Pro Ser Phe Leu Gln Ala Arg
 35
                         40
Ser Arg Pro Cys Leu Ser Gln Ala Cys Ser Pro Ala Ala Ser Val Leu
                  55
                                       60
Ser Ser Ser Ser Leu Cys Gly Arg Ser His Leu Leu Pro Gly Ser Leu
                 70
                                   75
Pro Ala Thr Ala Phe Leu Leu Leu Pro Gly Ser Leu Pro Gly Arg
              85
                                 90
                                                   95
Arg Pro Ser Ala Ala Gln Ala Ala Pro Val Leu Ala Trp Gly Leu Val
          100
                             105
Ala Phe Gln Leu Gly Val Ala Ala Gly Ala Gly Arg
       115
                          120
     <210> 393
     <211> 242
     <212> PRT
     <213> Rat
     <400> 393
Gly His Cys Asp Cys Gln Ala Gly Tyr Gly Gly Glu Ala Cys Gly Gln
                                 10
Cys Gly Leu Gly Tyr Phe Glu Ala Glu Arg Asn Ser Ser His Leu Val
                             25
         20
Cys Ser Ala Cys Phe Gly Pro Cys Ala Arg Cys Thr Gly Pro Glu Glu
       35
                          40
                                            45
```

Ser His Cys Leu Gln Cys Arg Lys Gly Trp Ala Leu His His Leu Lys

```
50
                       55
                                         60 ·
Cys Val Asp Ile Asp Glu Cys Gly Thr Glu Gln Ala Thr Cys Gly Ala
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Asn Thr Glu Gly Ser Tyr Arg Cys Val Cys Ala Glu Gly Phe Arg Gln 145 150 155 160
Glu Asp Gly Ile Cys Val Lys Glu Gln Ile Pro Glu Ser Ala Gly Phe
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Phe Ala Glu Met Thr Glu Asp Glu Met Val Val Leu Gln Gln Met Phe
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Phe Gly Val Ile Ile Cys Ala Leu Ala Thr Leu Ala Ala Lys Gly Asp
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Leu Val Phe Thr Ala Ile Phe Ile Gly Ala Val Ala Ala Met Thr Gly
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His Gly Asn 835			8	340				845		-	
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Cys Asn Met 865		870		•		875			_	_	880
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Leu Leu Thr	900			905		-		_	910		_
Val Thr Ile			9	920				925			
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Cys Pro Tyr 945		950				955					960
Cys Ile Ser	965			•	970					975	
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Glu Ser Cys			1	L000				1005	5		
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1010			1015								•
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Pro Pro Glu 1025 Ala Gln Asp Pro Lys Gly Cys Asp Ile 1007 Ala His Cys 1090 Gly Tyr Ser 1105 Arg Thr Ser Ile Ile Arg Gly Glu Lys 2115 Ser Tyr Leu 1170 Thr Leu Gln	Leu Asn 104 Phe Lys 1060 Asp Phe 5 Thr Asp Gly Leu Pro Cys 112 Val Asn 1140 Cys Glu 5 Gln Ile Ile Ala Asp His 120	Gly G 1030 Pro C 5 Cys F Asp F Ala V 1110 Asp F Glu F Pro S 1190 Ile F	Cys G Asp C Asp C 1095 Cys G Asn P Pro I Leu V 136er A 1175 Asp G	Sin His Cys Thr 1065 Cys Gin 080 Asn Gly Siu Phe Phe Asp 1149 Val Ser 1160 Ala Lys Siu Asp Val Glu	Asp 1050 Pro 5 Asp Tyr Cys Gln 6 Val Val Ser Leu 1210	Gly Asn Thr Pro 1115 Gln Cys Asn Arg Gly Tyr	Lys Lys Tyr Lys Cys 1100 Pro Asn Leu Phe 1180 Ile Arg	Leu Cys Ile Cys 1085 Val Met Gly Pro Val 1165 Gln Leu	Gly 1070 Lys Cys Val Ala Gly 1150 Asn Thr	Leu 1055 Glu Asn Pro Leu Gln 1135 Tyr Lys Asn Tyr Val 1215	104 Thr His His Gly Leu 112 Cys Leu Glu His Lys 120 Arg

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Trp Val Leu Asp Gly Lys Thr Trp Leu Lys Val Thr Leu Lys Glu Gln
    35 40
Ile Ser Lys Pro Asp Ser Gly Leu Val Ala Leu Lys Ala Glu Gly Gln
  50 55
                                     60
Asp Leu Leu Glu Leu Glu Lys Asn His Arg Leu Leu Ala Pro Gly
                                  75
        · 70
Tyr Thr Glu Thr Tyr Tyr Ser Arg Asp Gly Gln Pro Ile Val Leu Ser
            85
                              90
Pro Asn His Thr Asp His Cys His Tyr Gln Gly Cys Val Arg Gly Phe
         100 105 110
Arg Glu Ser Trp Val Val Leu Ser Thr Cys Ser Gly Met Ser Gly Leu
                        120
                                          125
Ile Val Leu Ser Ser Lys Val Ser Tyr Tyr Leu His Pro Trp Met Pro
                   135
                              140
Gly Asp Thr Lys Asp Phe Pro Thr His Lys Ile Phe Arg Val Glu Gln 145 150 150 155 160
Leu Phe Thr Trp Arg Gly Ala Arg Lys Asp Lys Asn Ser Gln Phe Lys
             165
                              170
                                                175
Ala Gly Met Ala Arg Leu Pro His Val Pro His Arg Arg Met Arg Arg
                         185
       180
                                           190
Glu Ala Arg Arg Ser Pro Lys Tyr Leu Glu Leu Tyr Ile Val Ala Asp
195 200 205
His Ala Leu Phe Leu Leu Gln Arg Gln Asn Leu Asn His Thr Arg Gln
                   215 . 220
Arg Leu Leu Glu Ile Ala Asn Cys Val Asp Gln Ile Leu Arg Thr Leu
                230
                                 235
Asp Ile Gln Leu Val Leu Thr Gly Leu Glu Val Trp Thr Glu Gln Asp
                              250
             245
His Ser Arg Ile Thr Gln Asp Ala Asp Glu Thr Leu Trp Ala Phe Leu
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260
                               265
                                                  270
Gln Trp Arg Arg Gly Leu Trp Val Arg Arg Pro His Asp Ser Thr Gln
      275
                         280
                                            285
Leu Leu Thr Gly Arg Thr Phe Gln Gly Thr Thr Val Gly Leu Ala Pro
                      295
                                         300
Val Glu Gly Met Cys His Ala Glu Ser Ser Gly Gly Val Ser Thr Asp
         310
305
                                    315
His Ser Glu Leu Pro Ile Gly Thr Ala Ala Thr Met Ala His Glu Ile
         325
                                330
                                                     335
Gly His Ser Leu Gly Leu His His Asp Pro Glu Gly Cys Cys Met Glu
           340
                            345
                                                 350
Ala Asp Ala Glu Gln Gly Gly Cys Val Met Glu Ala Ala Thr Gly His
                         360
                                   365
Pro Phe Pro Arg Val Phe Ser Ala Cys Ser Arg Arg Gln Leu Arg Thr
                       375
                                         380
Phe Phe Arg Lys Gly Gly Gly Ala Cys Leu Ser Asn Val Ser Ala Pro
                  390
                                    395
Gly Leu Leu Val Leu Pro Ser Arg Cys Gly Asn Gly Phe Val Glu Ala
              405
                                410
                                                    415
Glu Glu Glu Cys Asp Cys Gly Ser Gly Gln Lys Arg Pro Asp Pro Cys
          420
                           425
Cys Phe Ala His Asn Cys Ser Leu Arg Ala Gly Ala Gln Cys Ala Gln
     435
                       440
Gly Asp Cys Cys Ala Arg Cys Leu Leu Lys Pro Ala Gly Thr Pro Cys
   450
                    455
                                        460
Arg Pro Ala Ala Asn Asp Cys Asp Leu Pro Glu Phe Cys Thr Gly Thr 465 470 475 480
Ser Pro His Cys Pro Ala Asp Val Tyr Leu Leu Asp Gly Ser Pro Cys
485 490 495
              485
                                                    495
Ala Glu Gly Arg Gly Tyr Cys Leu Asp Gly Trp Cys Pro Thr Leu Glu 500 505 . 510
Lys Gln Cys Gln Gln Leu Trp Gly Pro Gly Ser Gln Pro Ala Pro Glu
      515
                          520
                                          525
Pro Cys Phe Gln Gln Met Asn Ser Val Gly Asn Ser Gln Gly Asn Cys
  530
        535
                                      540
Gly Gln Asp Ser Lys Gly Ser Phe Leu Pro Cys Thr Gln Arg Asp Ala
545 550 555 560
Gln Cys Gly Lys Leu Leu Cys Gln Gly Gly Lys Pro Asn Pro Leu Val
              565
                                570
Pro His Val Val Thr Val Asp Ser Thr Ile Leu Leu Glu Gly Arg Gln
                         585
         580
                                                590
Val Leu Cys Arg Gly Ala Phe Val Leu Pro Asp Thr His Leu Asp Gln
595 600 605
       595
                        600
                                         605
Leu Gly Leu Gly Leu Val Glu Pro Gly Thr Arg Cys Gly Pro Arg Met 610 615 620
Val Cys Gln Glu Arg His Cys Gln Asn Ala Thr Ser Gln Glu Leu Glu
                  630
                                    635 . 640
Arg Cys Ser Ser Gly Cys His Asn Arg Gly Val Cys Asn Ser Asn Arg
             645
                                 650
                                                   655
Asn Cys His Cys Ala Ala Gly Trp Ala Pro Pro Phe Cys Asp Lys Pro 660 665 670
Gly Leu Gly Gly Ser Val Asp Ser Gly Pro Ala Gln Ser Ala Asn Pro
       675
                          680
Asp Ala Phe Pro Leu Ala Met Leu Leu Ser Phe Leu Leu Pro Leu Leu
                     695
                           700
Pro Gly Ala Gly Leu Ala Trp Cys Tyr Tyr Gln Leu Pro Thr Leu Cys
                  710
                                    715
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Gln Gln Pro Gly Arg Cys Cys Arg Arg Asp Ala Leu Cys Asn Arg Asp
               725
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Gln Pro Leu Gly Ser Val His Pro Val Glu Phe Gly Ser Ile Ile Thr
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Gly Glu Pro Ser Pro Pro Asn Pro Glu Glu Ser Glu Leu Thr
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His Arg Val Tyr Val Gly Leu Phe Thr Gly Ser Ser Pro Asn Pro Phe
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                              25
                                                 30
Ala Glu Asp Val Lys Arg Pro Pro Glu Pro Leu Val Thr Asp Lys Glu
                         40
Ala Arg Lys Lys Val Leu Lys Gln Ala Phe Ser Val Ser Arg Val Pro
                     55
Glu Lys Leu Asp Ala Val Val Ile Gly Ser Gly Ile Gly Gly Leu Ala
                  70
Ser Ala Ala Ile Leu Ala Lys Ala Gly Lys Arg Val Leu Val Leu Glu
              85
                                 90
Gln His Thr Lys Ala Gly Gly Cys Cys His Thr Phe Gly Glu Asn Gly
           100
                              105
                                                 110
Leu Glu Phe Asp Thr Gly Ile His Tyr Ile Gly Arg Met Arg Glu Gly
      115
                         120
                                             125
Asn Ile Gly Arg Phe Ile Leu Asp Gln Ile Thr Glu Gly Gln Leu Asp
 130
                      135
                                         140
Trp Ala Pro Met Ala Ser Pro Phe Asp Leu Met Ile Leu Glu Gly Pro
                150
                            155.
Asn Gly Arg Lys Glu Phe Pro Met Tyr Ser Gly Arg Lys Glu Tyr Ile
165 170 175
Gln Gly Leu Lys Glu Lys Phe Pro Lys Glu Glu Ala Val Ile Asp Lys
          180
                            185
                                       190
Tyr Met Glu Leu Val Lys Val Val Ala His Gly Val Ser His Ala Ile
       195
                          200
                                             205
Leu Leu Lys Phe Leu Pro Leu Pro Leu Thr Gln Leu Leu Asn Lys Phe
   210
                     215 .
                                220
Gly Leu Leu Thr Arg Phe Ser Pro Phe Cys Arg Ala Ser Thr Gln Ser
                  230
                                    235
Leu Ala Glu Val Leu Lys Gln Leu Gly Ala Ser Pro Glu Leu Gln Ala
             245
                                 250
                                                    255
Val Leu Ser Tyr Ile Phe Pro Thr Tyr Gly Val Thr Pro Ser His Thr 260 265 270
Thr Phe Ser Leu His Ala Leu Leu Val Asp His Tyr Ile Gln Gly Ala 275 280 285
Tyr Tyr Pro Arg Gly Gly Ser Ser Glu Ile Ala Phe His Thr Ile Pro
                     295
                                        300
Leu Ile Gln Arg Ala Gly Gly Ala Val Leu Thr Arg Ala Thr Val Gln
                 310
                                     315 .
Ser Val Leu Leu Asp Ser Ala Gly Arg Ala Cys Gly Val Ser Val Lys
              325
                                 330
                                                    335
Lys Gly Gln Glu Leu Val Asn Ile Tyr Cys Pro Val Val Ile Ser Asn
           340
                              345
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Ala Gly Met Phe Asn Thr Tyr Gln His Leu Leu Pro Glu Ser Val Arg
      355
                       360
                                        365
Tyr Leu Pro Asp Val Lys Lys Gln Leu Thr Met Val Lys Pro Gly Leu
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                  375
                             380
Ser Met Leu Ser Ile Phe Ile Cys Leu Lys Gly Thr Lys Glu Glu Leu 385 390 395 400
              390
                                395
Lys Leu Gln Ser Thr Asn Tyr Tyr Val Tyr Phe Asp Thr Asp Met Asp 405 410 415
Lys Ala Met Glu Arg Tyr Val Ser Met Pro Lys Glu Lys Ala Pro Glu
        420
                  425
                                          430
His Ile Pro Leu Leu Phe Ile Ala Phe Pro Ser Ser Lys Asp Pro Thr
               440
                                445
Trp Glu Asp Arg Phe Pro Asp Arg Ser Thr Met Thr Val Leu Val Pro
             455
Thr Ala Phe Glu Trp Phe Glu Glu Trp Gln Glu Glu Pro Lys Gly Lys
               470
                      475
Arg Gly Val Asp Tyr Glu Thr Leu Lys Asn Thr Phe Leu Glu Ala Ser
                      490
           485
                                               495
Met Ser Val Ile Met Lys Leu Phe Pro Gln Leu Glu Gly Lys Val Glu 500 505 510
                                    510
Ser Val Thr Gly Gly Ser Pro Leu Thr Asn Gln Tyr Tyr Leu Ala Ala 515 520 520
                               525
His Arg Gly Ala Thr Tyr Gly Ala Asp His Asp Leu Ala Arg Leu His
 530 . 535
                                    540
Pro His Ala Met Ala Ser Leu Arg Ala Gln Thr Pro Ile Pro Asn Leu
545 550
                         555
Tyr Leu Thr Gly Gln Asp Ile Phe Thr Cys Gly Leu Met Gly Ala Leu
     565 570 575
Gln Gly Ala Leu Leu Cys Ser Ser Ala Ile Leu Lys Arg Asn Leu Tyr
        580 585
                                           590
Ser Asp Leu Gln Ala Leu Gly Ser Lys Val Arg Ala Gln Lys Lys
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Lys
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<211> 559

<212> PRT

<213> Rat

<400> 499

115

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Ser Val Arg Asp Gln Asp Ser Gly Asp Asn Gly Arg Ile Leu Cys Ser
   130
                   135
Ile Pro Asp Asp Leu Pro Phe Ile Leu Lys Pro Thr Phe Lys Asn Phe
145
              150
                               155
Phe Thr Leu Leu Ser Glu Lys Ala Leu Asp Arg Glu Ser Arg Ala Glu
            165
                      170
Tyr Asn Ile Thr Ile Thr Val Ser Asp Leu Gly Thr Pro Arg Leu Thr 180 . 185 . 190
Thr Gln His Thr Ile Thr Val Gln Val Ser Asp Ile Asn Asp Asn Ala
 195
                              205
                     200
Pro Ala Phe Thr Gln Thr Ser Tyr Thr Met Phe Val His Glu Asn Asn
        215
                           220
Ser Pro Ala Leu His Ile Gly Thr Ile Ser Ala Thr Asp Ser Asp Ser
                       235
       230
Gly Ser Asn Ala His Ile Thr Tyr Ser Leu Met Pro Pro Arg Asp Pro
            245
                           250
Gln Leu Ala Leu Asp Ser Leu Ile Ser Ile Asn Ala Asp Asn Gly Gln
          260
                          265
Leu Phe Ala Leu Arg Ala Leu Asp Tyr Glu Val Leu Gln Ala Phe Glu
     275
                    280
Phe Arg Val Gly Ala Thr Asp Arg Gly Ser Pro Ala Leu Ser Ser Gln 290 295 300
                            300
Ala Leu Val Arg Val Val Leu Asp Asp Asn Asp Asn Ala Pro Phe
305
       310
                       315
Val Leu Tyr Pro Leu Gln Asn Ala Ser Ala Pro Tyr Thr Glu Leu Leu
        325 330
Pro Arg Ala Ala Glu Pro Gly Tyr Leu Val Thr Lys Val Val Ala Val 340 345 350
                         345
Asp Arg Asp Ser Gly Gln Asn Ala Trp Leu Ser Phe Gln Leu Leu Lys
     355 360
                              365
Ala Thr Glu Pro Gly Leu Phe Ser Val Trp Ala His Asn Gly Glu Val
  370
                  375
                                   380
Arg Thr Ser Arg Leu Leu Ser Glu Arg Asp Ala Pro Lys His Lys Leu
              390
                              395
Leu Leu Met Val Lys Asp Asn Gly Asp Pro Pro Arg Ser Ala Ser Val
405 410 415
Met Leu His Val Leu Val Val Asp Gly Phe Ser Gln Pro Tyr Leu Pro
        420
                         425 . 430
Leu Pro Glu Val Ala His Asn Pro Ala His Asp Glu Asp Thr Leu Thr
 435
              440
                                       445
Ser Val Leu Leu Phe Val Gly Val Arg Leu Cys Lys Lys Ala Arg Ala
465 470
                              475 480
Ala Ser Leu Gly Gly Cys Ser Val Pro Glu Gly His Phe Pro Gly His
             485
                    490 495
Leu Val Asp Val Thr Gly Thr Gly Thr Leu Ser Gln Asn Tyr Gln Tyr
        500
                         505 510
Glu Val Cys Leu Thr Gly Ser Thr Gly Thr Asn Glu Phe Lys Phe Leu
      515
                      520
                                       525
Lys Pro Val Met Pro Ser Leu Gln Leu Gln Asp Pro Asp Ser Asn Met
                   535
   530
                                   540
Leu Val Lys Glu Asn Phe Arg Asn Ser Leu Gly Phe Asn Ile Gln
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425

420

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Pro Asn Gln Glu Thr Ser Phe Tyr Leu Val Gly Asn Leu Trp Leu Met
                  440
    435
                                           445
Ser Leu Lys Ala Leu Lys Tyr Arg Ser Met Lys Ile Thr Val Asn Ala
                             460
                   455
Ala Leu Gln Arg Gln Phe His Ser Pro Phe Ile Phe Arg Glu Glu Asp
                 470
                                 475
Pro Ser Arg Gln Val Thr Phe Glu Ile Ser Lys Gln Glu Asp Trp Gln
     485
                              490 495
Val Pro Ile Trp Ile Ile Val Gly Ser Ser Leu Gly Gly Leu Leu Leu
         500
                            505
                                              510
Leu Ala Leu Leu Val Leu Ala Leu Trp Lys Leu Gly Phe Phe Lys Ser
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                        520
Ala Lys Arg Lys Arg Glu Pro Ser Leu Gly Pro Val Pro Lys Glu Leu
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Val Tyr Asn Leu Arg Gln Asn Arg Phe Val Phe Asn Gly Thr Leu Lys
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                             25
Asp Ser His Ser Tyr Gln Asn Ala Arg Phe Gly Ser Cys Ile Ala Ser
                       40
                                        45
Val Gln Asp Leu Asn Gln Asp Ser Tyr Asn Asp Val Val Val Gly Ala
                     55
                                     60
Pro Leu Glu Asp Ser His Arg Gly Ala Ile Tyr Ile Phe His Gly Phe
                                   75
               70
Gln Thr Asn Ile Leu Lys Lys Pro Val Gln Arg Ile Ser Ala Ser Glu
            85
                                9.0
Leu Ala Pro Gly Leu Gln His Phe Gly Cys Ser Ile His Gly Gln Leu
          100 105
                                              110
Asp Leu Asn Glu Asp Gly Leu Val Asp Leu Ala Val Gly Ala Leu Gly
    115
               120
                                           125
Asn Ala Val Val Leu Trp Ala Arg Pro Val Val Gln Ile Asn Ala Ser 130 $135$
Leu His Phe Glu Pro Ser Lys Ile Asn Ile Phe His Lys Asp Cys Lys
                                   155
    150
Arg Asn Gly Arg Asp Ala Thr Cys Leu Ala Ala Phe Leu Cys Phe Gly
             165
                               170
                                                  175 .
Pro Ile Phe Leu Ala Pro His Phe His Thr Ala Thr Val Gly Ile Arg
         180
                          185
                                            190
Tyr Asn Ala Thr Met Asp Glu Arg Arg Tyr Met Pro Arg Ala His Leu 195 200 205
Asp Glu Gly Ala Asp Gln Phe Thr Asn Arg Ala Val Leu Leu Ser Ser
                    215
Gly Gln Glu His Cys Gln Arg Ile Asn Phe His Val Leu Asp Thr Ala
                230
                                 235
Asp Tyr Val Lys Pro Val Ala Phe Ser Val Glu Tyr Ser Leu Glu Asp
              245
                               250
                                                 255
Pro Asp His Gly Pro Met Leu Asp Asn Gly Trp Pro Thr Thr Leu Arg
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260
                           265
Val Ser Val Pro Phe Trp Asn Gly Cys Asn Glu Asp Glu His Cys Val
  275
              280
                                        285
Pro Asp Leu Val Leu Asp Ala Arg Ser Asp Leu Pro Thr Ala Met Glu
 290
                  295
                                     300
Thr Leu Ser Phe Asp Thr Thr Val Phe Ile Ile Glu Ser Thr Arg Arg
            325
                             330 335
Arg Val Ala Val Glu Ala Thr Leu Glu Asn Arg Gly Glu Asn Ala Tyr
          340
                           345
                                             350
Ser Ala Val Leu Asn Ile Ser Gln Ser Glu Asn Leu Gln Phe Ala Ser 355 360 365
Leu Ile Gln Lys Asp Asp Ser Asp Asn Ser Ile Glu Cys'Val Asn Glu
           375
                            . 380
  370
Glu Arg Arg Leu His Lys Lys Val Cys Asn Val Ser Tyr Pro Phe Phe
       390
                         395
Arg Ala Lys Ala Lys Val Ala Phe Arg Leu Asp Phe Glu Phe Ser Lys
          405
                              410
Ser Val Phe Leu His His Leu Gln Ile His Leu Gly Ala Gly Ser Asp
420 425 430
Ser His Glu Gln Asp Ser Thr Ala Asp Asp Asn Thr Ala Leu Leu Arg
                      440
                               445
Phe His Leu Lys Tyr Glu Ala Asp Val Leu Phe Thr Arg Ser Ser Ser
                    455
                                     460
Leu Ser His Phe Glu Val Lys Ala Asn Ser Ser Leu Glu Ser Tyr Asp
                470
                                 475
Gly Ile Gly Pro Pro Phe Asn Cys Val Phe Lys Val Gln Asn Leu Gly
          485
                              490
Phe Phe Pro Ile His Gly Val Met Met Lys Ile Thr Val Pro Ile Ala
         500
                           505
Thr Arg Gly Gly Asn Arg Leu Leu Met Leu Lys Asp Phe Phe Thr Asp
      515
                      520
                                         525
Gln Val Asn Thr Ser Cys Asn Ile Trp Gly Asn Ser Thr Glu Tyr Arg
 530
                   535
                                     540
Ser Thr Pro Thr Glu Glu Asp Leu Ser His Ala Pro Gln Arg Asn His
545 550 . 555
Ser Asn Ser Asp Val Val Ser Ile Ile Cys Asn Val Arg Leu Ala Pro
             565
                              570
                                            575
Asn Gln Glu Thr Ser Phe Tyr Leu Val Gly Asn Leu Trp Leu Met Ser
                         585
         580
                                            590
Leu Lys Ala Leu Lys Tyr Arg Ser Met Lys Ile Thr Val Asn Ala Ala
      595
                       600
Leu Gln Arg Gln Phe His Ser Pro Phe Ile Phe Arg Glu Glu Asp Pro
                   615
                                   620
Ser Arg Gln Val Thr Phe Glu Ile Ser Lys Gln Glu Asp Trp Gln Val
               630
                                635
Pro Ile Trp Ile Ile Val Gly Ser Ser Leu Gly Gly Leu Leu Leu 645 650 655
Ala Leu beu Val Leu Ala Leu Gly Ser Leu Val Ser Leu Lys Val Pro
                  665 670
        660
Ser Ala Arg Gly Ser Pro Ala Trp Ala Pro Ser Pro Lys Ser Trp Ser
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Glu Asp Pro Glu Glu Ala Ser Ser
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<210> 502

PCT/NZ01/00099 **WO** 01/90357

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> Ile Lys Gly Leu Asp Pro Asp Thr Asn Tyr Gln Phe Ala Val Arg Ala

Glu Leu Asp Leu Asp Val Ser Phe Glu Glu Val Lys Pro Leu Pro Ala $90 \hspace{1.5cm} 95$ Thr Lys Val Gly Asn Lys Lys Ser Lys Lys Thr Ser Val Ser Asn Ser

40 Arg Thr Leu Gly Pro Gly Glu Ala Gly Ser Gly Arg Tyr Gly Pro Gly 50 55 60 Tyr Ile Thr Asp Thr Gly Val Ser Glu Asp Asp Asp Ala Ser Glu Asp

70

25 Met Asn Ala Tyr Gly Phe Ser Leu Arg Ser Gln Pro Ser Asn Thr Ile

20

35

75

			100					105					110		
Glu	Met	Asp 115	Ser	Arg	Leu	Ala	Gln 120		Thr	Ser	Ala	Ser 125		Pro	Glu
	130					135					140			Lys	
145					150					155				Glu	160
Leu	Cys	Ser	Ala	Asp 165	Ser	Phe	Cys	Val	Asn 170	Asp	Tyr	Ala	Trp	Gly 175	Gly
			180					185	_	_			190	Ser	
		195					200					205		Val	
	210					215					220			Leu	
225					230					235				Glu	240
				245					250					Arg 255	
	_		260	•				265					270	Ile	
		275					280					285		Tyr	
	290					295		•			300			Val Pro	
305					310					315				Thr	320
				325					330			_		335	_
	٠	_	340			_	_	345					350	Asn	
		355					360					365		Asn	
	370					375					380			Ser	
385					390					395				Ile	400
				405					410					Phe 415 Ala	
			420					425					430	Phe	
	_	435					440					445		Ser	
	450					455			_		460		_	Gly	_
465					470					475		. •		Arg	480
				485				•	490					495 Ser	
			500					505		•		•	510	Val	
		515					520			-		525		Asp	
	530					535					540			Ser	
545	416	GTĀ	GTĀ	AGT	550	W211	TÄT	yab	usb	555	пÃг	пåэ	uoii	ser	560

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Ile Leu His Pro Phe Ser Gly Ser Ile Gln Lys Ile Ile Leu Asn Asp
                                570
              565
Arg Thr Ile His Val Arg His Asp Phe Thr Ser Gly Val Asn Val Glu
          580
                             585
                                                590
Asn Ala Ala His Pro Cys Val Gly Ala Pro Cys Ala His Gly Gly Ser
     595
                        600
                                       605
Cys Arg Pro Arg Lys Glu Gly Tyr Glu Cys Asp Cys Pro Leu Gly Phe 610 615 620
  610
                     61`5
                                        620
Glu Gly Leu Asn Cys Gln Lys Ala Ile Thr Glu Ala Ile Glu Ile Pro
               630
                                  635
Gln Phe Ile Gly Arg Ser Tyr Leu Thr Tyr Asp Asn Pro Asn Ile Leu
              645
                        650
Lys Arg Val Ser Gly Ser Arg Ser Asn Ala Phe Met Arg Phe Lys Thr
          660
                             665
Thr Ala Lys Asp Gly Leu Leu Leu Trp Arg Gly Asp Ser Pro Met Arg
675 680 685
Pro Asn Ser Asp Phe Ile Ser Leu Gly Leu Arg Asp Gly Ala Leu Val
                   695
                                        700
Phe Ser Tyr Asn Leu Gly Ser Gly Val Ala Ser Ile Met Val Asn Gly
                 710
                                    715
Ser Phe Ser Asp Gly Arg Trp His Arg Val Lys Ala Val Arg Asp Gly 725 730 735
Gln Ser Gly Lys Ile Thr Val Asp Asp Tyr Gly Ala Arg Thr Gly Lys 740 745 750
Ser Pro Gly Met Met Arg Gln Leu Asn Ile Asn Gly Ala Leu Tyr Val
     755
                        760
                                             765
Gly Gly Met Lys Glu Ile Ala Leu His Thr Asn Arg Gln Tyr Met Arg
  770 775 .
                               780
Gly Leu Val Gly Cys Ile Ser His Phe Thr Leu Ser Thr Asp Tyr His 785 790 795
                                  795
Ile Ser Leu Val Glu Asp Ala Val Asp Gly Lys Asn Ile Asn Thr Cys
                                 810
Gly Ala Lys
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     <212> PRT
     <213> Human
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Glu Gln Gly His Leu Arg Ser Leu Val Leu Gly Asp Asn Cys Leu Ser
       20
                            25
                                              30
Glu Asn Tyr Glu Glu Thr Ala Ala Ala Leu His Ala Leu Pro Gly Leu
     35
                        40
                                          45
Arg Arg Leu Asp Leu Ser Gly Asn Ala Leu Thr Glu Asp Met Ala Ala 50 55 60
Leu Met Leu Gln Asn Leu Ser Ser Leu Arg Ser Val Ser Leu Ala Gly
     70
Asn Thr Ile Met Arg Leu Asp Asp Ser Val Phe Glu Gly Leu Glu Arg
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Ile Ser Arg Arg Tyr Asp Cys Val Asp Ile Asn Glu Cys Thr Leu Asn
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Arg Lys Arg Leu Glu Glu Glu Lys Ser Glu Lys Ala Leu Arg Asn Glu
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Ser Phe Asp Leu Gly Val Cys Asp Trp Lys Gln Asp Arg Glu Asp Asp 405 410 415
Phe Asp Trp Asn Pro Ala Asp Arg Asp Asn Asp Val Gly Tyr Tyr Met 420 \hspace{1.5cm} 425 \hspace{1.5cm} 430
Ala Val Pro Ala Leu Ala Gly His Lys Lys Asn Ile Gly Arg Leu Lys 435 440 445
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Asp Tyr Arg Leu Ala Gly Asp Lys Val Gly Lys Leu Arg Val Phe Val 465 470 475 480
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Gly Lys Trp Lys Thr Gly Lys Val Pro Leu Tyr Gln Gly Ile Asp Thr 500 \hspace{1cm} 505 \hspace{1cm} 510
Thr Lys Ser Val Ile Phe Glu Ala Glu Arg Gly Lys Gly Lys Thr Gly
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Phe Lys Tyr Pro Trp Asn Ile Pro Phe Thr Val Gln Pro Gln Leu Leu
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205

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Leu Glu Val Arg Asp Ser Ile Gln Ser Cys Trp Val Leu Pro Trp Leu
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540

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1920

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Asp Ser His Ser Tyr Gln Asn Ala Arg Phe Gly Ser Cys. Ile Ala Ser
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                          40
Val Gln Asp Leu Asn Gln Asp Ser Tyr Asn Asp Val Val Gly Ala
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                                            60
Pro Leu Glu Asp Ser His Arg Gly Ala Ile Tyr Ile Phe His Gly Phe
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                                      75
Gln Thr Asn Ile Leu Lys Lys Pro Val Gln Arg Ile Ser Ala Ser Glu
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                                   90
                                                        95
Leu Ala Pro Gly Leu Gln His Phe Gly Cys Ser Ile His Gly Gln Leu
            100
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                                                110
Asp Leu Asn Glu Asp Gly Leu Val Asp Leu Ala Val Gly Ala Leu Gly
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Asn Ala Val Val Leu Trp Ala Arg Pro Val Val Gln Ile Asn Ala Ser
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Arg Asn Gly Arg Asp Ala Thr Cys Leu Ala Ala Phe Leu Cys Phe Gly
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Pro Ile Phe Leu Ala Pro His'Phe His Thr Ala Thr Val Gly Ile Arg
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Tyr Asn Ala Thr Met Asp Glu Arg Arg Tyr Met Pro Arg Ala His Leu
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Asp Glu Gly Ala Asp Gln Phe Thr Asn Arg Ala Val Leu Leu Ser Ser 210 215 220
Gly Gln Glu His Cys Gln Arg Ile Asn Phe His Val Leu Asp Thr Ala
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225 230
Asp Tyr Val Lys Pro Val Ala Phe Ser Val Glu Tyr Ser Leu Glu Asp
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Pro Asp His Gly Pro Met Leu Asp Asn Gly Trp Pro Thr Thr Leu Arg
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Val Ser Val Pro Phe Trp Asn Gly Cys Asn Glu Asp Glu His Cys Val
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Pro Asp Leu Val Leu Asp Ala Arg Ser Asp Leu Pro Thr Ala Met Glu
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                                       300
Tyr Cys Gln Gln Val Leu Arg Arg Pro Ala Gln Asp Cys Ser Ser Tyr
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Thr Leu Ser Phe Asp Thr Thr Val Phe Ile Ile Glu Ser Thr Arg Arg
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Arg Val Ala Val Glu Ala Thr Leu Glu Asn Arg Gly Glu Asn Ala Tyr
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                           345
                                               350
Ser Ala Val Leu Asn Ile Ser Gln Ser Glu Asn Leu Gln Phe Ala Ser
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Leu Ile Gln Lys Asp Asp Ser Asp Asn Ser Ile Glu Cys Val Asn Glu
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Glu Arg Arg Leù His Lys Lys Val Cys Asn Val Ser Tyr Pro Phe Phe 385 390 395 400
                               395
Arg Ala Lys Ala Lys Val Ala Phe Arg Leu Asp Phe Glu Phe Ser Lys
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Ser Val Phe Leu His His Leu Gln Ile His Leu Gly Ala Gly Ser Asp
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                                               430
Ser His Glu Gln Asp Ser Thr Ala Asp Asp Asn Thr Ala Leu Leu Arg
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                                           445
Phe His Leu Lys Tyr Glu Ala Asp Val Leu Phe Thr Arg Ser Ser Ser
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                     455
                               460
Leu Ser His Phe Glu Val Lys Ala Asn Ser Ser Leu Glu Ser Tyr Asp
465
                470
                                    475
Gly Ile Gly Pro Pro Phe Asn Cys Val Phe Lys Val Gln Asn Leu Gly
            485
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Phe Phe Pro Ile His Gly Val Met Met Lys Ile Thr Val Pro Ile Ala
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Thr Arg Gly Gly Asn Arg Leu Leu Met Leu Lys Asp Phe Phe Thr Asp
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Gln Val Asn Thr Ser Cys Asn Ile Trp Gly Asn Ser Thr Glu Tyr Arg
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Ser Thr Pro Thr Glu Glu Asp Leu Ser His Ala Pro Gln Arg Asn His
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Ser Asn Ser Asp Val Val Ser Ile Ile Cys Asn Val Arg Leu Ala Pro
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Asn Gln Glu Thr Ser Phe Tyr Leu Val Gly Asn Leu Trp Leu Met Ser
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Leu Lys Ala Leu Lys Tyr Arg Ser Met Lys Ile Thr Val Asn Ala Ala
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Leu Gln Arg Gln Phe His Ser Pro Phe Ile Phe Arg Glu Glu Asp Pro
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Ser Arg Gln Val Thr Phe Glu Ile Ser Lys Gln Glu Asp Trp Gln Val
625 630 ` 635
Pro Ile Trp Ile Ile Val Gly Ser Ser Leu Gly Gly Leu Leu Leu
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Ala Leu Leu Val Leu Ala Leu Trp Lys Leu Gly Phe Phe Lys Ser Ala
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Cys Ser Ala Cys Phe Gly Pro Cys Ala Arg Cys Thr Gly Pro Glu Glu
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Cys Val Asp Ile Asp Glu Cys Gly Thr Glu Gln Ala Thr Cys Gly Ala
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Asp Gln Phe Cys Val Asn Thr Glu Gly Ser Tyr Glu Cys Arg Asp Cys
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                              90
Ala Lys Ala Cys Leu Gly Cys Met Gly Ala Gly Pro Gly Arg Cys Lys
100 105 110
Lys Cys Ser Arg Gly Tyr Gln Gln Val Gly Ser Lys Cys Leu Asp Val
     115 120
                                     125
Asp Glu Cys Glu Thr Val Val Cys Pro Gly Glu Asn Glu Gln Cys Glu
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                                    140
Asn Thr Glu Gly Ser Tyr Arg Cys Val Cys Ala Glu Gly Phe Arg Gln
              150
                                155
Glu Asp Gly Ile Cys Val Lys Glu Gln Ile Pro Glu Ser Ala Gly Phe
            165
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                                               175
Phe Ala Glu Met Thr Glu Asp Glu Met Val Val Leu Gln Gln Met Phe
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                         185 · 190
Phe Gly Val Ile Ile Cys Ala Leu Ala Thr Leu Ala Ala Lys Gly Asp
 195
              200
                               205,
Leu Val Phe Thr Ala Ile Phe Ile Gly Ala Val Ala Ala Met Thr Gly 210 215 220
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<213> Rat

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85 90 95 Val Val Glu Val Leu Gln Asp Asn Val Asp Phe Asp Ile Asp Val Asn 100 105 110 Ala Ser Val Phe Glu Thr Asn Ile Arg Val Val Gly Gly Leu Leu Ser 115 120 125 Ala His Leu Leu Ser Lys Lys Ala Gly Val Glu Val Glu Ala Gly Trp 130 135 140 Pro Cys Ser Gly Pro Leu Leu Arg Met Ala Glu Glu Ala Ala Arg Lys 145 150 155 Leu Leu Pro Ala Phe Gln Thr Pro Thr Gly Met Pro Tyr Gly Thr Val 165 170 175 Asn Leu Leu His Gly Val Asn Pro Gly Glu Thr Pro Val Thr Cys Thr 180 185 190 Ala Gly Ile Gly Thr Phe Ile Val Glu Phe Ala Thr Leu Ser Ser Leu . 200 195 Thr Gly Asp Pro Val Phe Glu Asp Val Ala Arg Val Ala Leu Met Arg 210 . 215 220 Leu Trp Glu Ser Arg Ser Asp Ile Gly Leu Val Gly Asn His Ile Asp 230 235 Val Leu Thr Gly Lys Trp Val Ala Gln Asp Ala Gly Ile Gly Ala Gly 250 245 Val Asp Ser Tyr Phe Glu Tyr Leu Val Lys Gly Ala Ile Leu Leu Gln 260 265 270 265 Asp Lys Lys Leu Met Ala Met Phe Leu Glu Tyr Asn Lys Ala Ile Arg 280 275 285 Asn Tyr Thr His Phe Asp Asp Trp Tyr Leu Trp Val Gln Met Tyr Lys 290 295 300 Gly Thr Val Ser Met Pro Val Phe Gln Ser Leu Glu Ala Tyr Trp Pro 305 310 315 320 Gly Leu Gln Ser Leu Ile Gly Asp Ile Asp Asn Ala Met Arg Thr Phe 325 330 Leu Asn Tyr Tyr Thr Val Trp Lys Gln Phe Gly Gly Leu Pro Glu Phe 340 345 Tyr Asn Ile Pro Gln Gly Tyr Thr Val Glu Lys Arg Glu Gly Tyr Pro 355 360 365 Leu Arg Pro Glu Leu Ile Glu Ser Ala Met Tyr Leu Tyr Arg Ala Thr 370 375 200 375 Gly Asp Pro Thr Leu Leu Glu Leu Gly Arg Asp Ala Val Glu Ser Ile 385 390 395 . 400 Glu Lys Ile Ser Lys Val Glu Cys Gly Phe Ala Thr Ile Lys Asp Leu 405 410 415 Arg Asp His Lys Leu Asp Asn Arg Met Glu Ser Phe Phe Leu Ala Glu 420

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Thr Val Lys Tyr Leu Tyr Leu Leu Phe His Pro Asn Asn Phe Ile His
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Asn Asn Gly Ser Thr Phe Asp Ser Val Met Thr Pro His Gly Glu Cys
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Ile Leu Gly Ala Gly Gly Tyr Ile Phe Asn Thr Glu Ala His Pro Ile
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Asp Pro Ala Ala Leu His Cys Cys Arg Arg Leu Lys Glu Glu Gln Trp 485 490 495
Glu Val Glu Asp Leu Ile Lys Glu Phe Tyr Ser Leu Arg Gln Ser Arg
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Ala Gly Pro Gly Thr Leu Ser Ser Pro Glu Asn Gln Pro Arg Glu Lys
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Gln Pro Ala Arg Gln Arg Ala Pro Leu Leu Ser Cys Pro Ser Gln Pro
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Glu Asn Asn Glu Leu Trp Lys Lys Val Glu Thr Leu Glu Thr Ala Asn
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Arg Thr Leu Leu Gln Gln Leu Gln Lys Leu Gln Thr Leu Val Thr Ser
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Lys Ile Ser Arg Pro Tyr Lys Met Ala Ala Thr Gln Thr Gly Thr Cys 65 70 75 80
Leu Met Val Ala Ala Leu Cys Phe Val Leu Val Leu Gly Ser Leu Ala
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Pro Cys Leu Pro Ala Phe Ser Ser Gly Ser Lys Thr Val Lys Glu Asp
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Pro Val Ala Ala Asp Ser Val Tyr Ala Ala Ser Gln Met Pro Ser Arg
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Ser Leu Leu Phe Tyr Asp Asp Gly Ala Gly Ser Trp Glu Asp Gly His
130 135 140
Arg Gly Ala Leu Leu Pro Val Glu Pro Pro Glu Gly Trp Glu Leu Lys
145
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Pro Gly Gly Pro Ala Glu Pro Arg Pro Gln Asp His Leu Arg His Asp
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            165
His Ala Asp Ser Ile His Glu Thr Thr Lys Tyr Leu Arg Glu Thr Trp
180 185 190
Pro Glu Asp Thr Glu Asp Asn Gly Ala Ser Pro Asn Phe Ser His Pro
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Lys Glu Trp, Phe His Asp Arg Asp Leu Gly Pro Asn Thr Thr Ile Lys
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Leu Ser
225
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Leu Arg Pro Phe Cys Leu His Thr Gly Cys Ala Gly Cys Ser Leu Arg
  35
                       40
Ala Ala Thr Glu Gln Cys Ala Val Ala Leu Ala Pro Gln Leu Pro Ser
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Thr Arg
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Arg Arg Gln Pro Pro Pro Lys Asp Gln Arg Glu Arg Ala Arg Ala Gly
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Ser Leu Ser Leu Gly Ala Leu Tyr Thr Ala Ala Ile Val Ala Phe Val
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Leu Phe Lys Cys Leu Gln Gln Gly Pro Asp Glu Ala Ala Val Pro Arg
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Glu Glu Lys Asn Lys Lys Ser Ser Gln Ser Glu Gln Gln Leu Val
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Gln Leu Thr Gln Gln Leu Ala Gln Thr Glu Glu His Leu Asn Asn Leu
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Met Thr Gln Leu Asp Pro Leu Phe Glu Arg Val Thr Thr Leu Val Gly
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Thr Gln Arg Glu Leu Leu Asn Ala Lys Leu Lys Thr Ile His His Leu
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Leu Gln Asp Cys Lys Pro Gly Ile Gly Val Glu Ala Pro Glu Pro Glu
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Ala Pro Ile His Phe Pro Glu Asp Leu Gly Lys Glu Asp. Gln Glu Asp
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                           185
Ala Gly Asn Ser Gln Ala Trp Glu Glu Pro Ile Asn Trp Ser Ser Glu
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Thr Trp Asn Leu Ala Pro Ser Trp Glu Val Glu Gln Gly Leu Arg Arg
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Arg Trp His Lys Thr Lys Gly Pro Ala Val Asn Gly Gly Gln Ala Leu
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Lys Val
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Ile Cys Ser Ile Pro Gly Leu Pro Gly Pro Pro Gly Pro Pro Gly Ala
                         40
Asn Gly Ser Pro Gly Pro His Gly Arg Ile Gly Leu Pro Gly Arg Asp
                    55
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Gly Arg Asp Gly Arg Lys Gly Glu Lys Gly Glu Lys Gly Thr Ala Gly
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                                    75
Leu Lys Gly Lys Thr Gly Pro Leu Gly Leu Ala Gly Glu Lys Gly Asp
              85
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                                                   95
Gln Gly Glu Thr Gly Lys Lys Gly Pro Ile Gly Pro Glu Gly Glu Lys
          100
                            105
                                              110
Gly Glu Val Gly Pro Ala Gly Pro Pro Gly Pro Lys Gly Asp Arg Gly
     115
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                                           125
Asp Gln Gly Asp Pro Gly Leu Pro Gly Val Cys Arg Cys Gly Ser Ile
  130
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Val Leu Lys Ser Ala Phe Ser Val Gly Ile Thr Thr Ser Tyr Pro Glu
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                                    155
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Glu Arg Leu Pro Ile Ile Phe Asn Lys Val Leu Phe Asn Glu Gly Glu
             165
                                170
                                                   175
His Tyr Asn Pro Ala Thr Gly Lys Phe Ile Cys Ala Phe Pro Gly Ile
                            185
                                              190
Tyr Tyr Phe Ser Tyr Asp Ile Thr Leu Ala Asn Lys His Leu Ala Ile
   195
                         200
                                           205
Gly Leu Val His Asn Gly Gln Tyr Arg Ile Arg Thr Phe Asp Ala Asn
  210
                     215
                                      220
Thr Gly Asn His Asp Val Ala Ser Gly Ser Thr Val Ile Tyr Leu Gln 225 230 235
225
                  230
                                    235
                                                        240
Pro Glu Asp Glu Val Trp Leu Glu Ile Phe Phe Asn Asp Gln Asn Gly
            245
                                250
Leu Phe Ser Asp Pro Gly Trp Ala Asp Ser Leu Phe Ser Gly Phe Leu
    260
                           265
                                               270
Leu Tyr Val Asp Thr Asp Tyr Leu Asp Ser Ile Ser Glu Asp Asp Glu
                         280
                                            285
Leu
<210> 631
<211> 213
<212> PRT
<213> Rat
<400> 631
Met Val Leu Gly Gly Cys Pro Val Ser Tyr Leu Leu Leu Cys Gly Gln
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                                                   15
Ala Ala Leu Leu Gly Asn Leu Leu Leu His Cys Val Ser Arg
         20
                            25
                                              30
Ser His Ser Phe Asn Ala Thr Ala Glu Leu Asp Leu Thr Pro Ser Gly
      35
                          40
```

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Ala Ala His Leu Glu Gly Pro Ala Ala Ser Ser Trp Glu Tyr Ser Asp
                     55
                                    60
Pro Asn Ser Pro Val Ile Leu Cys Ser Tyr Leu Pro Asp Glu Phe Val
                  70
                                  75
Asp Cys Asp Ala Pro Val Asp His Val Gly Asn Ala Thr Ala Tyr Gln
             85
                              90
Glu Leu Gly Tyr Gly Cys Leu Lys Phe Gly Gly Gln Ala Tyr Ser Asp
          100
                          105
                                             110
Val Glu His Thr Ala Val Gln Cys Arg Ala Leu Glu Gly Ile Glu Cys
     115 120
Ala Ser Pro Arg Thr Phe Leu Arg Lys Asn Lys Pro Cys Ile Lys Tyr
                              140
 130
        135
Thr Gly His Tyr Phe Ile Thr Thr Leu Leu Tyr Ser Phe Phe Leu Gly 145 150 150 160
Cys Phe Gly Val Asp Arg Phe Cys Leu Gly His Thr Gly Thr Ala Val
            165 170 175
Gly Lys Leu Leu Thr Leu Gly Gly Leu Gly Ile Trp Trp Phe Val Asp
       180
                        185
                                    190
Leu Ile Leu Leu Ile Thr Gly Gly Leu Met Pro Ser Asp Gly Ser Asn
   195
                        200
                                          205
Trp Cys Thr Val Tyr
  210
<210> 632
<211> 167
<212> PRT
<213> Rat
<400> 632
Met Ala Ser Pro Arg Thr Ile Thr Ile Val Ala Leu Ser Val Ala Leu
             5
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Gly Leu Phe Phe Val Phe Met Gly Thr Ile Lys Leu Thr Pro Arg Leu
       20
                            25
                                             30
Ser Lys Asp Ala Tyr Ser Glu Met Lys Arg Ala Tyr Lys Ser Tyr Val$35$ 40 45
Arg Ala Leu Pro Leu Leu Lys Lys Met Gly Ile Asn Ser Ile Leu Leu
 50 55
                                    60
Arg Lys Ser Ile Gly Ala Leu Glu Val Ala Cys Gly Ile Val Met Thr
                                 75
             70
Leu Val Pro Gly Arg Pro Lys Asp Val Ala Asn Phe Phe Leu Leu Leu
            85
                            90
Leu Val Leu Ala Val Leu Phe Phe His Gln Leu Val Gly Asp Pro.Leu
         100
                           105
                                             110
Lys Arg Tyr Ala His Ala Leu Val Phe Gly Ile Leu Leu Thr Cys Arg
              120
                                   125
Leu Leu Ile Ala Arg Lys Pro Glu Asp Arg Ser Phe Glu Lys Lys Ala
 130
                   135
                                   140 - '
Leu Pro Glu Ser Ala Glu Glu Gln Pro Ser Leu Tyr Glu Lys Ala Pro
     150
Gln Gly Lys Val Lys Val Ser
              165
<210> 633
<211> 138
<212> PRT
<213> Rat
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Phe Ile Arg Gly Met Leu Lys Leu Ile Leu Leu Leu Phe Ser Gly
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Ala Thr Leu Ser Ser Thr Trp Phe Thr Leu Thr Cys Leu Asn Ser Val
         20
                           25
                                              30
Thr His Leu Pro Leu Thr Thr Val Thr Leu Tyr Ala Ser Cys Ile Leu
      35
                      40
                                         45
Leu Gly Val Phe Leu Asn Ser Ser Val Pro Ile Phe Phe Glu Leu Phe
  50
               55
Val Glu Thr Val Tyr Pro Val Pro Glu Gly Ile Thr Cys Gly Val Val
               70 ·
                                   75
Thr Phe Leu Ser Asn Met Phe Met Gly Val Leu Leu Phe Phe Val Thr
                              90
             85
Phe Tyr His Thr Glu Leu Ser Trp Phe Asn Trp Cys Leu Pro Gly Ser
        100 105 110
Cys Leu Leu Ser Leu Leu Leu Ile Leu Cys Phe Arg Glu Ser Tyr Asp
   115
                      120
Arg Leu Tyr Leu Asp Val Val Val Ser Val
 130 135
<210> 634
<211> 75
<212> PRT
<213> Rat
<400> 634
Met Ile Gly Asp Ile Leu Leu Phe Gly Thr Leu Leu Met Asn Ala Gly
               5
                  10
Ala Val Leu Asn Phe Lys Leu Lys Lys Lys Asp Thr Gln Gly Phe Gly
         20
                           25
                                            30
Glu Glu Ser Arg Glu Pro Ser Thr Gly Asp Asn Ile Arg Glu Phe Leu
     35
                        40
                                         45
Leu Ser Leu Arg Tyr Phe Arg Ile Phe Ile Ala Leu Trp Asn Val Phe
 50
                   55
Met Met Leu Cys Met Ile Val Leu Phe Gly Ser
65
                 70
<210> 635
<211> 186
<212> PRT
<213> Rat
<400> 635
Met Val Ala Ala Val Ala Thr Ala Trp Leu Leu Leu Trp Ala Ala Ala
              5
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Cys Thr Gln Ser Glu Gln Asp Phe Tyr Asp Phe Lys Ala Val Asn Ile
      20
                           25
Arg Gly Lys Leu Val Ser Leu Glu Lys Tyr Arg Gly Ser Val Ser Leu
      35
                        40
                                         45
Val Val Asn Val Ala Ser Glu Cys Gly Phe Thr Asp Gln Asn Tyr Arg
                   55
                                60
Ala Leu Gln Gln Leu Gln Arg Asp Leu Gly Pro Tyr His Phe Asn Val
                 70
                                  75
Leu Ala Phe Pro Cys Asn Gln Phe Gly Gln Glu Pro Asp Ser Asn
             85
                             90
Arg Glu Ile Glu Asn Phe Ala Arg Arg Thr Tyr Ser Val Ser Phe Pro
          100
                            105,
                                              110
```

```
Met Phe Ser Lys Ile Ala Val Thr Gly Thr Gly Ala His Pro Ala Phe
      115
                      120
                                        125
Lys Tyr Leu Thr Gln Thr Ser Gly Lys Glu Pro Thr Trp Asn Phe Trp
 130
                    135
                                     140
Lys Tyr Leu Val Ala Pro Asp Gly Lys Val Val Gly Ala Trp Asp Pro
145
                150
                              155
                                                  160
Thr Val Pro Val Glu Glu Ile Lys Pro Arg Ile Thr Glu Gln Val Met 165 170 175
Lys Leu Ile Leu Gln Lys Arg Glu Asp Leu
         180
                          185
<210> 636
<211> 930
<212> PRT
<213> Rat
<400> 636
Met Pro Ser Leu Leu Ser Leu Val Leu Thr Phe Leu Ala Val Ser Ser
          5
                            10
Pro Ser Cys Cys Gln Asn Ser Asp Thr Ala Ser Pro Lys Ala Ser Asn 20 25 30
Gly Ala Ser Phe Leu Trp Asn Asn Met Arg Leu Pro Glu Tyr Ile Thr
    35 40 45
Pro Ile His Tyr Asp Leu Met Ile His Ala Asn Leu Ser Thr Leu Thr
                 55
                             . 60
Phe Trp Gly Lys Thr Glu Val Glu Ile Thr Val Ser Gln Pro Thr Ser
              70
                         75
Thr Ile Ile Met His Ser His Gln Leu Gln Ile Ser Lys Ala Thr Leu
             85
                             90 95
Arg Arg Gly Ala Glu Glu Met Leu Pro Glu Glu Pro Leu Lys Leu Met
         100
                         105 110
Glu Tyr Ser Ala His Glu Gln Val Ala Leu Leu Thr Ala Gln Pro Leu
 115
                     120
                                        125
Leu Ala Gly Ser Val Tyr Thr Val Ile Ile Thr Tyr Ala Ala Asn Leu
130 135 140
Ser Glu Asn Phe His Gly Phe Tyr Lys Ser Thr Tyr Arg Thr Gln Glu
145 150 155
Gly Glu Arg Arg Ile Leu Ala Ala Thr Gln Phe Glu Pro Thr Ala Ala
             165
                             170
                                      175
Arg Met Ala Phe Pro Cys Phe Asp Glu Pro Ala Leu Lys Ala Ser Phe
         180 185 190
Ser Ile Lys Ile Lys Arg Asp Pro Arg His Leu Ala Ile Ser Asn Met 195 200 205
Pro Leu Val Lys Ser Val Thr Val Ala Glu Gly Leu Ile Glu Asp His
  210
             215
                            220
Phe Asp Ile Thr Val Lys Met Ser Thr Tyr Leu Val Ala Phe Ile Ile
225
              230
                                 235
Ser Asp Phe Lys Ser Val Ser Lys Met Thr Lys Ser Gly Val Lys Val 245 250 255
Ser Val Tyr Ala Val Pro Asp Lys Ile Asn Gln Ala Asp Tyr Ala Leu
         260 265 270
Asp Ala Ala Val Thr Leu Leu Glu Phe Tyr Glu Asp Tyr Phe Ser Ile
      275 ·
             280 . 285
Pro Tyr Pro Leu Pro Lys Gln Asp Leu Ala Ala Ile Pro Asp Phe Gln
  290
            295 300
Ser Gly Ala Met Glu Asn Trp Gly Leu Thr Thr Tyr Arg Glu Ser Ala
305
                         , 315
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Leu Leu Tyr Asp Lys Glu Lys Ser Ser Ala Ser Ser Lys Leu Gly Ile
               325
                               330
                                       · 335
Thr Met Thr Val Ser His Glu Leu Ala His Gln Trp Phe Gly Asn Leu
           340
                          345
                                       350
Val Thr Met Glu Trp Trp Asn Asp Leu Trp Leu Asn Glu Gly Phe Ala
                        360
                                     365
Lys Phe Met Glu Phe Val Ser Val Thr Val Thr His Pro Glu Leu Lys
                     375
                                       380
Val Glu Glu Tyr Phe Phe Gly Lys Cys Val Asn Ala Met Glu Val Asp
              390
                                    395
Ala Leu Asn Ser Ser His Pro Val Ser Thr Pro Val Glu Asn Pro Ala
             405
                              410
Gln Ile Arg Glu Met Phe Asp Glu Val Ser Tyr Glu Lys Gly Ala Cys
          420
                425
Ile Leu Asn Met Leu Arg Asp Tyr Leu Ser Ala Asp Thr Phe Lys Arg
      435
                       440
Gly Ile Val Gln Tyr Leu Gln Lys Tyr Ser Tyr Lys Asn Thr Lys Asn
  450
                   455
                                       460
Glu Asp Leu Trp Asn Ser Met Met His Ile Cys Pro Thr Asp Gly Thr
               470
                                    475
Gln Thr Met Asp Gly Phe Cys Ser Arg Asn Gln His Ser Ser Ser Thr 485 490 495
Ser His Trp Arg Gln Glu Val Ile Asp Ile Lys Ser Met Met Asn Thr
                          505 . 510
         500
Trp Thr Leu Gln Lys Gly Phe Pro Leu Ile Thr Ile Thr Val Arg Gly
                        520
                                           525
Arg Asn Val His Leu Lys Gln Glu His Tyr Met Lys Gly Ser Glu Cys
            535
                                      540
Phe Pro Glu Thr Gly Ser Leu Trp His Val Pro Leu Thr Phe Ile Thr 545 550 555 . 560
545 550
Ser Lys Ser Asp Ser Val Gln Arg Phe Leu Leu Lys Thr Lys Thr Asp
              565
                                570
                                                   575
Val Ile Ile Leu Pro Glu Ala Val Glu Trp Ile Lys Phe Asn Val Gly
                                       590
         580
                            585
Met Asn Gly Tyr Tyr Ile Val His Tyr Gly Asp Asp Gly Trp Ala Ser 595 600 605
                                           605
Leu Asn Gly Leu Leu Lys Glu Ala His Thr Thr Ile Ser Ser Asn Asp
                    615
                                      620
Arg Ala Ser Leu Ile Asn Asn Ala Phe Gln Leu Val Ser Ile Gly Lys
                 630
                                    635
Leu Ser Ile Glu Lys Ala Leu Asp Leu Ile Leu Tyr Leu Lys Asn Glu
              645
                                650
Thr Glu Ile Met Pro Ile Phe Gln Gly Leu Asn Glu Leu Ile Pro Met
          660
                             665
Tyr Lys Leu Met Glu Lys Arg Asp Met Val Glu Val Glu Thr Gln Phe
     675
                        680
                                            685
Lys Asp Phe Leu Leu Arg Leu Leu Lys Asp Leu Ile Asn Lys Gln Thr
 690
                    695
                                      700
Trp Thr Asp Glu Gly Ser Val Ser Glu Arg Met Leu Arg Ser Gln Leu 705 710 715 720
Leu Leu Leu Ala Cys Val His Arg Tyr Gln Leu Cys Val Gln Arg Ala 725 730 735
Glu Arg Tyr Phe Arg Glu Trp Lys Ala Ser Asn Gly Asn Met Ser Leu
          740
                             745
                                              750
Pro Ile Asp Val Thr Leu Ala Val Phe Ala Val Gly Ala Gln Asn Thr
       755
                        760
Glu Gly Trp Asp Phe Leu Tyr Ser Lys Tyr Gln Ser Ser Leu Ser Ser
```

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770
                     775
                                      780
Thr Glu Lys Ser Gln Ile Glu Phe Ser Leu Cys Ile Ser Gln Asp Pro
785
         790
                          795
Glu Lys Leu Gln Trp Leu Leu Asp Gln Ser Phe Lys Gly Glu Ile Ile
             805
                              810
Lys Thr Gln Glu Phe Pro His Ile Leu Thr Leu Ile Gly Arg Asn Pro
                  825
         820
                                             830
Val Gly Tyr Pro Leu Ala Trp Lys Phe Leu Lys Glu Asn Trp Asn Lys
      835
              840
                                        845
Ile Val Gln Lys Phe Glu Leu Gly Ser Ser Ser Ile Ala His Met Val
            855
 850
                               860
Met Gly Thr Thr Asn Gln Phe Ser Thr Arg Ala Arg Leu Glu Glu Val
865
       870
                                  875
Lys Gly Phe Phe Ser Ser Leu Lys Lys Asn Gly Ser Gln Leu Arg Cys 885 890 895
Val Gln Gln Thr Ile Glu Thr Ile Glu Glu Asn Ile Arg Trp Met Asp
        900
                         905
                                             910
Lys Asn Phe Asp Lys Ile Arg Leu Trp Leu Gln Lys Glu Arg Gln Glu
                       920
Leu Leu
   930
<210> 637
<211> 161
<212> PRT
<213> Rat
<400> 637
Met Ala Tyr His Ser Gly Tyr Gly Val His Ala Met Ala Phe Ile Thr
             5 .
                             10
Tyr Val Leu Leu Ala Gly Met Ala Leu Gly Ile Gln Gln Arg Phe Ser
       20
                           25
                                             30
Pro Glu Val Leu Gly Leu Cys Ala Ser Thr Ala Leu Val Trp Val Leu
     35
                      40
Met Glu Val Leu Ala Leu Leu Leu Gly Leu Tyr Leu Ala Thr Val Arg
. 50 55
                               60
Ser Glu Leu Gly Thr Phe His Leu Leu Ala Tyr Ser Gly Tyr Lys Tyr
65
             70
                                 75
Val Gly Met Ile Leu Ser Val Leu Thr Gly Leu Leu Phe Gly Ser Asp
           85
                            90
Gly Tyr Tyr Val Ala Leu Ala Trp Thr Ser Ser Ala Leu Met Tyr Phe
              105 110
         100
Thr Val Arg Ser Leu Arg Thr Ala Ala Ser Gly Pro Asp Ser Met Gly
     115
                            125
                      120
Gly Pro Thr Pro Arg Gln His Leu Gln Leu Tyr Leu Thr Leu Gly Ala
 130
                   135
                                    140
Ala Ala Phe Gin Pro Leu Ile Ile Tyr Trp Leu Thr Phe His Leu Val
145
                 150
                                  155
Arg
<210> 638
<211> 165
<212> PRT
<213> Rat
<400> 638
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Met Ala Arg Ala Ala Gly Ile Thr Ala Ala Ile Thr Leu Ala Leu Leu
               5
                                  10
Gly Val Leu Ala Leu Gly Ala Gly Asp Gly Asp Phe Arg Leu Asp Asp
          20
                              25
                                                 30
Ala Leu Glu Asp Thr Asp Lys Lys Pro Thr Pro Lys Pro Pro Thr Pro
                         40
                                             45
Lys Lys Pro Ser Ser Gly Asp Phe Asp Leu Glu Glu Ala Leu Thr Gly 50 55 . 60
Gly Ala Asp Glu Asp Pro Arg Arg Pro Gly Ser Arg Pro Lys Pro Asp
65
                  70
Pro Lys Pro Pro Gly Pro Pro Arg Asp Ser Gly Gly Ile Ser Asp Arg
            85
                                 90
Asp Leu Glu Asp Val Ala Gly His Gly Gly Arg Gly Gly Gly Ala Gly
          100
                     105
Asp Arg Gly Thr Asp Gly Ala Glu Ser Glu Gly Gln Pro Gln Gly Leu
      115
                       120
                                           125
Ile Pro Gly Val Val Ala Ala Val Leu Ala Ala Leu Ala Gly Ala Val
 130
                   135
                                        140
Ser Ser Phe Val Ala Tyr Gln Lys Arg Arg Leu Cys Phe Arg Glu Gly
                  150
                                      155
Gly Ser Ala Pro Val
              165
<210> 639
<211> 61
<212> PRT
<213> Rat
<400> 639 .
Met His Ile Tyr Lys Tyr Val His Ile Asn Tyr Tyr Leu His Leu His
                                 10
Ile Cys Ile Tyr Val Tyr Thr His Ile Ser Val Gly Met Cys Ile Arg
          20
                              25
                                                 30
Ile Cys Leu Pro Ser Ser Ser His Trp Lys Lys Glu Ser Ile Arg Ser
 35
                         40
Gly Gly Ser Lys Asn Ala His Tyr Pro Gly Ser Gly Ile
 50
                      55
<210> 640
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<212> PRT
<213> Rat
<400> 640
Met Cys Phe Ser Leu Cys Ser Val Glu Val Phe Phe Leu Lys Gln Asn
                                 10
                                               . 15
Ser Asn Leu Leu Pro Ala His Ile Phe Ile Arg Ala Ser Pro Ile Cys
       20
Ile Ile Gly Asn Glu Tyr Glu Tyr Ile Phe Met Tyr Val Cys Asn His
     35
                        40
                                            45
Arg Ser His Leu Tyr Leu Gly Phe Ala Ala Ala Asp Tyr Phe Phe Pro
  50
                    55
                                          60 ·
His His Gly Thr Gly Asn Cys Phe Gln
65
                  70
<210> 641
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<213> Rat
<400> 641
Met Pro Val Leu Trp Leu Leu Leu Leu Pro Leu Pro Leu Pro Leu Leu 1 5 10 15
Ala Met Leu Cys Gln Gln Arg`Ser Pro Gly Ala Arg Pro Cys Trp Leu
 20
                           25
Ile Ser Leu Gln His Arg Val Ala Cys Val Val Leu Ser Trp Ala Ala
    35
                        40
                                          45
Ala Trp Gln Arg Arg Lys Leu Glu Gln Ser Thr Leu Asn Val Ser Gln
                    55
                                     60
Ser Gln Gln Gln Ala Leu Met Gly Cys Leu Lys Glu Ala Gln Gly Ser
                70
                                 75
Cys Cys Leu Pro Arg Glu Asn Thr Asp Met Thr Thr Phe Arg Asn Leu
            85
                                90
Pro Leu Thr Lys Thr Ser His Thr Gln Gln Lys Glu Ser Glu Glu Lys
         100
                    105
Leu Leu Pro Pro Thr Leu Pro Gln Tyr His Gly Asp Ala Ser Leu Gln
                120
                                 125
     115
Val Thr Leu Leu Gly Leu Met Thr Leu Asn Lys Ala Tyr Pro Glu Val
  130 135
                                      140
Leu Ala Pro Gly Ser Thr Ala Cys Val Thr Pro Thr Ser Pro Trp Pro
145
             150 .
                                   155
Tyr Ser Val Pro Trp Leu Gly His Ala Leu Gly Arg Val Ser Pro Ile
            165
                              170
Gly Ala Lys Asp Ala Arg Thr Leu Leu Leu Glu Ala Leu Ile Ser Pro
180 185 190
Gly Leu Arg Val Leu Glu Ala Arg Thr Ala Val Glu Leu Leu Asp Val
                       200
      195
                                          205
Phe Val Gly Leu Glu Ala Asp Gly Glu Glu Leu Ala Glu Val Ile Ala
                     215
                                        220
Ser Gly Ser Leu Gly Lys Leu Pro Arg Arg Ala Ala Glu Leu Gln Glu
225 230 235 240
         230
                                   235
Ala Leu Glu Gln Gly Pro Arg Gly Leu Ala Leu Arg Leu Trp Pro Lys
245 250 255
              245
                               250
Leu Gln Val Val Val Thr Leu Asp Ala Gly Gly Gln Ala Glu Ala Val
          260
                            265
                                              270
Ala Ala Leu Arg Val Leu Trp Cys Gln Gly Leu Ala Phe Phe Ser Pro
               280
    275
                                      285
Ala Tyr Ala Ala Ser Gly Gly Val Met Ala Ile Asn Leu Trp Pro Glu 290 295 300
                     295
Gln Pro Gln Gly Ser Tyr Leu Leu Ser Pro Gly Val Pro Phe Ile Glu
                                  315
               310
Leu Leu Pro Ile Lys Glu Gly Thr Gln Glu Glu Ala Ala Ser Thr Leu
             325
                               330
                                         335
Leu Leu Thr Asp Val Arg Arg Glu Glu Lys Tyr Glu Leu Val Leu Thr
          340
                     . 345
Asp Ser Thr Ser Leu Thr Arg Cys Arg Leu Gly Asp Val Val Gln Val 355 360 365
Ile Gly Thr Tyr Asn Gln Cys Pro Val Val Arg Phe Thr Cys Arg Leu
  370
                     375
                                       380
Gly Gln Thr Leu Ser Val Arg Gly Glu Val Thr Asp Glu Asn Val Phe
                390
                                   395
Ser Val Ala Leu Ala Gln Ala Val Gly Gln Cys Gln Gly Pro Ser Cys
                                . 410
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Trp Thr Met Ser Val Trp Arg Ala Thr Phe Trp Thr Pro Met Arg Asp
         420
                       425
Pro Pro His Thr Thr Lys Cys Leu Trp Ser
      435
                      440
<210> 642
<211> 65
<212> PRT
<213> Rat
<400> 642
Met Thr Val Cys Thr Leu Leu Val Ala Lys Ser Thr Leu Leu Leu Ser
                           10
Leu Ser Cys Leu Leu Cys Ser Leu Phe Leu Tyr Ser Val Ser Gly
 20
                     25
                                 30.
Ser Tyr Ser Arg Cys Pro Val Arg Trp Leu Val Cys Leu Ser Ser Gln
             40 .
 35
Leu Pro Trp Ala Thr Ser Gln Ser Leu Leu Lys Arg Lys Leu Ser Met
                   55
                                   60
65
<210> 643
<211> 197
<212> PRT
<213> Rat
<400> 643
Pro Arg Pro Gly Arg Ala Arg Thr Leu Arg Ser Pro Ser Gly Ser Arg
1 5
                10
Val Val Gln Arg Pro Arg Asn Asp Gly Val Ala Ala Leu Thr Gly Ala
      20
                         25
                                          30
Gly Gly Cys Arg Ala Pro Arg Ala Gly Met Ala Gly Gln Phe Arg Ser
     35
                   40
                                      45
Tyr Val Trp Asp Pro Leu Leu Ile Leu Ser Gln Ile Val Leu Met Gln \, 50 \, 55 \, 60
Thr Val Tyr Tyr Gly Ser Leu Gly Leu Trp Leu Ala Leu Val Asp Ala
            70 75
Leu Val Arg Ser Asn Pro Ser Leu Asp Gln Met Phe Asp Ala Glu Ile
            85
                            90
Let Gly Phe Ser Thr Pro Pro Gly Arg Let Ser Met Met Ser Phe Val
        100 105 110
Leu Asn Ala Leu Thr Cys Ala Leu Gly Leu Leu Tyr Phe Ile Arg Arg
     115
                    120
                                     125
Gly Lys Gln Cys Leu Asp Phe Thr Val Thr Val His Phe Phe His Leu
 130 135 140
Leu Gly Cys Trp Leu Tyr Ser Ser Arg Phe Pro Ser Ala Leu Thr Trp
              150 155 160
Trp Leu Val Gln Ala Val Cys Ile Ala Leu Met Ala Val Ile Gly Glu
                     170 175
           165
Tyr Leu Cys Met Arg Thr Glu Leu Lys Glu Ile Pro Leu Ser Ser Ala
        180
                    185
                                 190
Pro Lys Ser Asn Val
     195
<210> 644
<211> 930
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<212> PRT

<213> Rat <400> 644 Met Pro Ser Leu Leu Ser Leu Val Leu Thr Phe Leu Ala Val Ser Ser Pro Ser Cys Cys Gln Asn Ser Asp Thr Ala Ser Pro Lys Ala Ser Asn 20 ` Gly Ala Ser Phe Leu Trp Asn Asn Met Arg Leu Pro Glu Tyr Ile Thr Pro Ile His Tyr Asp Leu Met Ile His Ala Asn Leu Ser Thr Leu Thr Phe Trp Gly Lys Thr Glu Val Glu Ile Thr Val Ser Gln Pro Thr Ser Thr Ile Ile Met His Ser His Gln Leu Gln Ile Ser Lys Ala Thr Leu Arg Arg Gly Ala Glu Glu Met Leu Pro Glu Glu Pro Leu Lys Leu Met Glu Tyr Ser Ala His Glu Gln Val Ala Leu Leu Thr Ala Gln Pro Leu Leu Ala Gly Ser Val Tyr Thr Val Ile Ile Thr Tyr Ala Ala Asn Leu Ser Glu Asn Phe His Gly Phe Tyr Lys Ser Thr Tyr Arg Thr Gln Glu Gly Glu Arg Arg Ile Leu Ala Ala Thr Gln Phe Glu Pro Thr Ala Ala Arg Met Ala Phe Pro Cys Phe Asp Glu Pro Ala Leu Lys Ala Ser Phe Ser Ile Lys Ile Lys Arg Asp Pro Arg His Leu Ala Ile Ser Asn Met Pro Leu Val Lys Ser Val Thr Val Ala Glu Gly Leu Ile Glu Asp His Phe Asp Ile Thr Val Lys Met Ser Thr Tyr Leu Val Ala Phe Ile Ile Ser Asp Phe Lys Ser Val Ser Lys Met Thr Lys Ser Gly Val Lys Val Ser Val Tyr Ala Val Pro Asp Lys Ile Asn Gln Ala Asp Tyr Ala Leu Asp Ala Ala Val Thr Leu Leu Glu Phe Tyr Glu Asp Tyr Phe Ser Ile Pro Tyr Pro Leu Pro Lys Gln Asp Leu Ala Ala Ile Pro Asp Phe Gln 290 295 300 Ser Gly Ala Met Glu Asn Trp Gly Leu Thr Thr Tyr Arg Glu Ser Ala 305 310 315 Leu Leu Tyr Asp Lys Glu Lys Ser Ser Ala Ser Ser Lys Leu Gly Ile Thr Met Thr Val Ser His Glu Leu Ala His Gln Trp Phe Gly Asn Leu Val Thr Met Glu Trp Trp Asn Asp Leu Trp Leu Asn Glu Gly Phe Ala 355 360 365 Lys Phe Met Glu Phe Val Ser Val Thr Val Thr His Pro Glu Leu Lys 375 · 380 Val Glu Glu Tyr Phe Phe Gly Lys Cys Phe Asn Ala Met Glu Val Asp Ala Leu Asn Ser Ser His Pro Val Ser Thr Pro Val Glu Asn Pro Ala Gln Ile Arg Glu Met Phe Asp Glu Val Ser Tyr Glu Lys Gly Ala Cys

```
420
                             425
Ile Leu Asn Met Leu Arg Asp Tyr Leu Ser Ala Asp Thr Phe Lys Arg
      435
                        440
                                          445
Gly Ile Val Gln Tyr Arg Gln Lys Tyr Ser Tyr Lys Asn Thr Lys Asn
       455
                                     460
  450
Glu Asp Leu Trp Asn Ser Met Met His Ile Cys Pro Thr Asp Gly Thr
465
       470
                                475
Gln Thr Met Asp Gly Phe Cys Ser Arg Asn Gln His Ser Ser Ser Thr
                        490
           485
Ser His Trp Arg Gln Glu Val Ile Asp Ile Lys Ser Met Met Asn Thr
          500
                           505
                                             510 /
Trp Thr Leu Gln Lys Gly Phe Pro Leu Ile Thr Ile Thr Val Arg Gly
      515
                      520
                                         525
Arg Asn Val His Leu Lys Gln Glu His Tyr Met Lys Gly Ser Glu Cys
           535
                             540
530
Phe Pro Glu Thr Gly Ser Leu Trp His Val Pro Leu Thr Phe Ile Thr
                550
                               555
Ser Lys Ser Asp Ser Val Gln Arg Phe Leu Leu Lys Thr Lys Thr Asp
                        570
                                                 575
           565
Val Ile Ile Leu Pro Glu Ala Val Glu Trp Ile Lys Phe Asn Val Gly
  580
                          585
                                              590
Met Asn Gly Tyr Tyr Ile Val His Tyr Gly Asp Asp Gly Trp Ala Ser
  595 600
                                          605
Leu Asn Gly Leu Leu Lys Glu Ala His Thr Thr Ile Ser Ser Asn Asp
 610
                    615
                                       620
Arg Ala Ser Leu Ile Asn Asn Ala Phe Gln Leu Val Ser Ile Gly Lys
                630
                                  635
Leu Ser Ile Glu Lys Ala Leu Asp Leu Ile Leu Tyr Leu Lys Asm Glu
             645
                        650
Thr Glu Ile Met Pro Ile Phe Gln Gly Leu Asn Glu Leu Ile Pro Met
          660
                           665
                                              670
Tyr Lys Leu Met Glu Lys Arg Asp Met Val Glu Val Glu Thr Gln Phe
                680
    675 .
                                          685
Lys Asp Phe Leu Leu Arg Leu Leu Lys Asp Leu Ile Asn Lys Gln Thr 690 695 700
Trp Thr Asp Glu Gly Ser Val Ser Glu Arg Met Leu Arg Ser Gln Leu
               710 . 715 720
Leu Leu Ala Cys Val His Arg Tyr Gln Leu Cys Val Gln Arg Ala
             725
                               730
Glu Arg Tyr Phe Arg Glu Trp Lys Ala Ser Asn Gly Asn Met Ser Leu
         740
                          745
Pro Ile Asp Val Thr Leu Ala Val Phe Ala Val Gly Ala Gln Asn Thr 755 \phantom{000}760 \phantom{000}765
Glu Gly Trp Asp Phe Leu Tyr Ser Lys Tyr Gln Ser Ser Leu Ser Ser
  770
             775
                                      780
Thr Glu Lys Ser Gln Ile Glu Phe Ser Leu Cys Ile Ser Gln Asp Pro.
               790
                                 795
Glu Lys Leu Gln Trp Leu Leu Asp Gln Ser Phe Lys Gly Glu Ile Ile
805 810 815
Lys Thr Gln Glu Phe Pro His Ile Leu Thr Leu Ile Gly Arg Asn Pro
                          825
                                              830
Val Gly Tyr Pro Leu Ala Trp Lys Phe Leu Lys Glu Asn Trp Asn Lys
      835
                        840
                                           845
Ile Val Gln Lys Phe Glu Leu Gly Ser Ser Ser Ile Ala His Met Val
                    855
                            860
Met Gly Thr Thr Asn Gln Phe Ser Thr Lys Ala Arg Leu Glu Lys Val
865
                  870
                            , 875
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Lys Gly Phe Phe Ser Ser Leu Lys Lys Asn Gly Phe Gln Leu Arg Cys
                                                  895
                                890
             885
Val Gln Gln Thr Ile Glu Thr Ile Glu Lys Asn Ile Arg Trp Met Asp
           900
                          905
                                               910
Lys Asn Phe Asp Lys Ile Arg Leu Trp Leu Gln Lys Lys Arg Gln Glu
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                                            925
Leu Leu
  930
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Met Leu His Asn Val Ser Lys Gly Val Val Tyr Ser Ala Thr Val Val
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Leu Gly Leu Leu Ala Tyr Val Ala Phe Lys Cys Trp Arg Ser Arg Lys
                                            30
  20
                           25
Gln Arg Gln Gln Leu Ala Lys Ala Arg Thr Val Glu Leu Gly Asp Pro
 35
                        40
                                 . 45
Asp Arg Asp Gln Arg His Gly Asp Ser Ser Ile Phe Val Asp Ser Pro
                   55
                                      60
His Gly Leu Glu Pro Cys Ile Pro Ser Gln Gly Pro His Ala Asp Leu
                  70
                                    75
Gly Cys Arg Leu Tyr Leu His Ile Pro Gln Gln Gln Gln Glu Glu Val
             85
                             90
                                                  95
Gln Arg Leu Leu Ile Leu Gly Glu Pro Ala Lys Gly Trp Gln Gly Leu 100 105 110
Ala Gly Gln Leu Gly Tyr Gln Ala Glu Ala Val Glu Thr Met Ala Cys
      115 120 125
Asp Gln Asp Pro Ala Tyr Ala Leu Leu Arg Asp Trp Ala Ala Gln Glu
130 135 140
Gly Ser Gly Ala Thr Leu Arg Val Leu Glu Asp Ala Leu Thr Ala Ile
145 150 160
Gly Arg Glu Asp Val Val Gln Val Leu Ser Ser Pro Ala Glu Gly Cys
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Ser Val Val
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Met Lys Tyr Leu Leu Asp Leu Ile Leu Leu Pro Leu Leu Ile Val
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Phe Cys Ile Glu Ser Phe Ile Lys Arg Leu Ile Pro Lys Lys Lys
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                                              30
Ser Val Ala Gly Glu Ile Val Leu Ile Thr Gly Ala Gly His Gly Ile
    35
                         40
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Gly Arg Leu Thr Ala Tyr Glu Phe Ala Lys Leu Asn Thr Lys Leu Val
                  55
                                    60
 50
Leu Trp Asp Ile Asn Lys Asn Gly Ile Glu Glu Thr Ala Ala Lys Cys
                  70
                                   75
Arg Lys Leu Gly Ala Gln Val His Pro Phe Val Val Asp Cys Ser Gln
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90
Arg Glu Glu Ile Tyr Ser Ala Val Arg Lys Val Lys Glu Glu Val Gly
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                  105
Asp Val Ser Ile Leu Val Asn Asn Ala Gly Val Val Tyr Thr Ala Asp
 115
                120
                                        125
Leu Phe Ala Thr Gln Asp Pro Gln Ile Glu Lys Thr Phe Glu Val Asn
130 135 140
            135
                                      140
Val Leu Ala His Phe Trp Thr Thr Lys Ala Phe Leu Pro Ala Met Met
145 150
                         155
Lys Asn Asn His Gly His Val Val Thr Val Ala Ser Ala Ala Gly His
            165
                             170
                                                175
Thr Val Val Pro Phe Leu Leu Ala Tyr Cys Ser Ser Lys Phe Ala Ala
                          185
         180
                                            190
Val Gly Phe His Arg Ala Leu Thr Asp Glu Leu Ala Ala Leu Gly Cys
195 200 205
                                        205
Thr Gly Val Arg Thr Ser Cys Leu Cys Pro Asn Phe Ile Asn Thr Gly
  210 215 .
                            220
Phe Ile Lys Asn Pro Ser Thr Asn Leu Gly Pro Thr Leu Glu Pro Glu
         . 230
                                  235
Glu Val Val Glu His Leu Met His Gly Ile Leu Thr Asn Gln Lys Met 245 250 255
Ile Phe Val Pro Gly Ser Ile Ala Leu Leu Thr Val Leu Glu Arg Val
        260
                 265 270
Phe Pro Glu Arg Phe Leu Asp Val Leu Lys His Arg Ile Asn Val Lys
  275
                  280
                                          285
Phe Asp Ala Val Val Gly Tyr Lys Asp Lys
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                     295
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Leu Ile Leu Pro Gly Val Glu Ala Val Glu Ala Gly Asp Ala Ile Ala
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                           25
Leu Leu Gly Val Val Leu Ser Val Thr Gly Ile Cys Ala Cys Leu
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Gly Ile Tyr Ala Arg Lys Arg Asn Gly Gln Ile
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<211> 281
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Val Leu Ser Thr Ala Pro Pro Thr Met Arg Pro Ala Pro Gln Pro Gln
1 5
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Asp Cys Pro Ala Ser Ile Cys Leu Asn Gly Gly Ser Cys Arg Val Gly
         20
                           25
                                       · 30
Ala Lys His His Leu Glu Cys Leu Cys Pro Glu Gly Phe Ile Gly Leu
                      40
                                        45
Tyr Cys Glu Ser Pro Val Glu Gln Arg Thr Lys Pro Ser Ser Ile Pro
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Asp Thr Pro Arg Pro Pro Arg Leu Leu Pro Leu Arg Ile Glu Pro Val
65
        70
                                 75
Ser Pro Thr Ser Leu Arg Val Glu Leu Gln Arg Tyr Leu Gln Gly Asn
            85 ·
                      90
                                               95
Thr Val Gln Leu Arg Ser Leu Arg Leu Thr Tyr Arg Asn Leu Ser Gly
        100 105
                                    110
Pro Asp Lys Arg Leu Val Thr Leu Arg Leu Pro Ala Ser Leu Ala Glu
115 120 125
Tyr Thr Val Thr Gln Leu Arg Pro Asn Ala Thr Tyr Ser Ile Cys Val
  130 135 140
Thr Ala Leu Gly Ala Gly Arg Thr Pro Glu Gly Glu Glu Ala Cys Gly 145 150 155 160
Glu Ala Asn Thr Pro Gln Ala Val Arg Ser Asn His Ala Pro Val Thr 165 170 175
Gln Ala Arg Glu Gly Asn Leu Pro Leu Leu Ile Ala Pro Ala Leu Ala
                  185
        180
                                    190
Ala Val Leu Leu Ala Val Leu Ala Ala Ser Gly Ala Val Tyr Cys Val
     195
               200
                                      205
Arg Arg Ala Arg Ala Ser Ser Thr Ala Gln Asp Lys Gly Gln Val Gly
 210 · 215
                                     220
Pro Gly Thr Gly Pro Leu Glu Leu Glu Gly Val Lys Val Pro Leu Glu
225 230 235 240
        230
225
                                 235
Pro Gly Ser Lys Ala Ser Glu Gly Gly Gly Glu Ala Leu Ser Gly Gly
            245
                             250 . 255
Pro Glu Cys Glu Val Pro Leu Met Gly Tyr Pro Gly Pro Ser Leu Gln
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Gly Val Leu Pro Ala Gln Pro Tyr Ile
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Leu Gly Ser Val Ser Val Thr Thr Ile Glu Pro Cys Val Gln Val Gly
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Ser Pro Ala Arg His Ser Leu His Pro Pro Leu Cys Ile Ser Ile Gly
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                           25
                                             30
Ala Thr Val Pro Tyr Phe Ala Glu Gly Ser Gly Gly Pro Val Pro Thr
 35
                     40
                                         45
Thr Ser Ala Leu Ile Leu Pro Pro Glu Tyr Ser Ser Trp Gly Tyr Pro
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                  55
                                    60
Tyr Glu Ala Pro Pro Ser Tyr Glu Gln Ser Cys Gly Ala Gly Gly Thr
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Asp Val Gly Leu Ile Pro Gly Ser
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Glu Val Asp Pro Asp Leu Lys Cys Ala Leu Cys His Lys Val Leu Glu
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Asp Pro Leu Thr Thr Pro Cys Gly His Val Phe Cys Ala Gly Cys Val
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30

20

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Leu Pro Trp Val Val Gln Glu Gly Ser Cys Pro Ser Arg Cys Arg Gly
                        40
     35
                                         45
Arg Leu Ser Ala Lys Glu Leu Asn His Val Leu Pro Leu Lys Arg Leu
                     55
Ile Leu Lys Leu Asp Ile Lys Cys Ala His Ala Ala Arg Gly Cys Gly 65 70 75 80
Arg Val Val Lys Leu Gln Asp Leu Pro Glu His Leu Glu Arg Cys Asp
85 90 95
Phe Ala Pro Ala Arg Cys Arg His Ala Gly Cys Gly Gln Leu Leu
                         105
                                       110
        100
Arg Arg Asp Val Glu Ala His Met Arg Asp Ala Cys Asp Ala Arg Pro
                    120
                                   125
      115
Val Gly Arg Cys Gln Glu Gly Cys Gly Leu Pro Leu Thr His Gly Glu
130 135 140
Gln Arg Ala Gly Gly His Cys Cys Ala Arg Ala Leu Arg Ala His Asn
145 150
                           155
Gly Ala Leu Gln Ala Arg Leu Gly Ala Leu His Lys Ala Leu Lys Lys
            165
                                170
Glu Ala Leu Arg Ala Gly Lys Arg Glu Lys Ser Leu Val Ala Gln Leu
                   185
         180
Ala Ala Gln Leu Glu Leu Gln Met Thr Ala Leu Arg Tyr Gln Lys
195 200 205
Lys Phe Thr Glu Tyr Ser Ala Arg Leu Asp Ser Leu Ser Arg Cys Val
                   215
                                       220
Ala Ala Pro Pro Gly Gly Lys Gly Glu Glu Thr Lys Ser Val Thr Leu
              230
                             235
Val Leu His Arg Asp Ser Gly Ser Leu Gly Phe Asn Ile Ile Gly Gly 245 250 255
Arg Pro Cys Val Asp Asn Gln Asp Gly Ser Ser Ser Glu Gly Ile Phe
        260
                           265
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Val Ser Lys Ile Val Asp Ser Gly Pro Ala Ala Lys Lys Arg Pro Ala
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Asn Ser
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Met Ala Arg Pro Arg Pro Arg Glu Tyr Lys Ala Gly Asp Leu Val Phe
1 5
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Ala Lys Met Lys Gly Tyr Pro His Trp Pro Ala Arg Ile Asp Glu Leu
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                             25
Pro Glu Gly Ala Val Lys Pro Pro Ala Asn Lys Tyr Pro Ile Phe Phe
      35
                       40
                                          45
Phe Gly Thr His Glu Thr Ala Phe Leu Gly Pro Lys Asp Leu Phe Pro 50 55 60
Tyr Lys Glu Tyr Lys Asp Lys Phe Gly Lys Ser Asn Lys Arg Lys Gly
                                   75
                70
Phe Asn Glu Gly Leu Trp Glu Ile Glu Asn Asn Pro Gly Val Lys Phe
              85
                                90
Thr Gly Tyr Gln Thr Ile Gln Gln Ser Ser Ser Glu Thr Glu Gly
                                               110
          100
                            105
Glu Gly Gly Asn Thr Ala Asp Ala Ser Ser Glu Glu Glu Gly Asp Arg
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120
Val Glu Asp Gly Lys Gly Lys Arg Lys Asn Glu Lys Gly Gly Ser Lys
                    135
 130
                                      140
Arg Lys Lys Ser Tyr Thr Ser Lys Lys Ser Ser Lys Gln Ser Arg Lys
               150
                           155
Ser Pro Gly Asp Glu Asp Asp Lys Asp Cys Lys Glu Glu Glu Asn Lys
165 170 175
Ser Ser Ser Glu Gly Gly Asp Ala Gly Asn Asp Thr Arg Asn Thr Thr
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Ser Asp Leu Gln Lys Ala Gly Glu Gly Thr
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<213> Rat
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Met Pro Val Ala Val Gly Pro Tyr Gly Gln Ser Gln Pro Ser Cys Phe
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Asp Arg Val Lys Met Gly Phe Val Met Gly Cys Ala Val Gly Met Ala
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Ala Gly Ala Leu Phe Gly Thr Phe Ser Cys Leu Arg Ile Gly Met Arg
     35
                        40 .
Gly Arg Glu Leu Met Gly Gly Ile Gly Lys Thr Met Met Gln Ser Gly
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                                       60
Gly Thr Phe Gly Thr Phe Met Ala Ile Gly Met Gly Ile Arg Cys
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<211> 555
<212> PRT
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<400> 653
Met Pro Val Asn Leu Gly Gln Ala Leu Gly Leu Leu Pro Phe Leu Ala
1 5
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Lys Ala Glu Asp Ala Thr Phe Ser Gly Ser Asp Val Ile Gln Gln Arg
         20
                            25
                                            30
Glu Leu Ala Asn Pro Glu Thr Ala Arg Gln Leu Phe Arg Gln Phe Arg
    35
                   40
                                     45
Tyr Gln Val Met Ser Gly Pro Gln Glu Thr Leu Arg Gln Leu Arg Lys
            55
                                      60
Leu Cys Phe Gln Trp Leu Arg Pro Glu Val His Thr Lys Glu Gln Ile
                70
Leu Glu Ile Leu Met Leu Glu Gln Phe Leu Thr Ile Leu Pro Gly Glu
             85
                               90
                                         ٠· 95
Ile Gln Met Trp Val Arg Lys.Gln Cys Pro Gly Ser Gly Glu Glu Ala 100 105 110
Val Thr Leu Val Glu Ser Leu Lys Gly Asp Pro Gln Lys Leu Trp Gln 115 120 125
                       120
Trp Ile Ser Ile Gln Val Leu Gly Gln Glu Ile Pro Phe Glu Lys Glu
  130
               135
                                      140 -
Asn Ser Ala Arg Cys Arg Gly Asp Lys Val Glu Pro Ala Leu Glu Ala
                150
                          155 160
Glu Pro Thr Val Glu Val Val Pro Gln Asp Leu Pro Leu Gln Asn Thr
                              . 170
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Ser Ser Ala Pro Gly Glu Leu Leu Ser His Gly Val Lys Glu Glu Ser
         180
                           185
                                              190
Asp Met Glu Pro Glu Leu Ala Leu Ala Ala Ser Gln Leu Pro Ala Arg
     195
                        200
                                         205
Ser Glu Glu Arg Pro Thr Arg Asp Gln Glu Val Gly Thr Ala Leu Leu
                   215
 210
                                     220
Pro Ser Leu Gln Glu Gln Gln Trp Arg His Leu Asp Ser Thr Gln Lys
                 230
                                  235
Glu Gln Tyr Trp Asp Leu Met Leu Glu Thr Tyr Gly Lys Met Val Ser
             245
                              250
Gly Ala Gly Ile Ser Asn Ser Lys Pro Asp Leu Thr Asn Met Ala Glu
          260
                  265
                                              270
Tyr Gly Glu Glu Leu Val Gly Leu His Leu His Ser Ala Glu Lys Met 275 280 285
Ala Arg Ala Pro Cys Lys Glu Asp Arg Gln Glu Asn Asp Lys Glu Asn
 290 . 295
                                      300
Leu Asn Leu Glu Asn His Arg Asp Gln Gly Cys Leu Asp Val Phe Asp
305 310
                                   315
Gln Ala Pro Gly Glu Ala Pro Pro Gln Thr Ala Leu Ser Asp Phe Phe
            325
                       330 335
Gly Glu Ser Glu Pro His His Phe Gly Gly Glu Ser Val Pro Glu Ala
        340
                                            350
                           345
Leu Glu Asn Leu Gln Gly Glu Gly Thr Gly Ala His Leu Phe Pro His
                       360
                                         365
Glu Arg Gly Ser Gly Lys Gln Leu Gly Gln His Ile Gln Ser Ser Ser
                    375
                                       380
Ser Gly Glu Leu Ser Ala Leu Trp Leu Glu Glu Lys Arg Glu Ala Ser
        . 390
                                   395
Gln Lys Gly Gln Ala Arg Ala Pro Met Ala Gln Lys Leu Pro Thr Cys
           . 405
                      410
Arg Glu Cys Gly Lys Thr Phe Tyr Arg Asn Ser Gln Leu Val Phe His
                           425
          420
                                     430
Gln Arg Thr His Thr Gly Glu Thr Tyr Phe His Cys Arg Ile Cys Lys
                       440
      435
                                         445
Lys Ala Phe Leu Arg Ser Ser Asp Phe Val Lys His Gln Arg Thr His
450 455 460
                455
Thr Gly Glu Lys Pro Cys Lys Cys Asp Tyr Cys Gly Lys Gly Phe Ser 465 470 475 480
Asp Phe Ser Gly Leu Arg His His Glu Lys Ile His Thr Gly Glu Lys 485 490 495
Pro Tyr Lys Cys Pro Ile Cys Glu Lys Ser Phe Ile Gln Arg Ser Asn
                   505
                                     510
Phe Asn Arg His Gln Arg Val His Thr Gly Glu Lys Pro Tyr Lys Cys
     515
                        520
                                   525
Thr His Cys Gly Lys Arg Phe Ser Trp Ser Ser Ser Leu Asp Lys His
                    535 540
Gln Arg Ser His Leu Gly Lys Lys Pro Cys Pro
545
                 550
                                    555
<210> 654
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<400> 654
Leu Ala Tyr Tyr Asn Pro Phe Tyr Phe Leu Ser Ala Ala Ala Pro Gly
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Pro Gly Ala Ala Thr Ser Ala Gly Ala Thr Pro Thr Ala Val Ala Gly
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                             25
Leu Thr Ala Arg Ala Pro His Val Gln Ala Ser Ala Arg Ala Val Pro
      35
                         40
Val Thr Arg Val Gly Ser Ala Ala Pro Ala Arg Thr Ala Ser Asp Thr
                    55
Gly Arg Gln Ala Gly Arg Glu Tyr Val Ile Pro Ser Leu Ala His Arg
                  70
                                   75
Phe Met Ala Glu Met Val Asp Phe Phe Ile Leu Phe Phe Ile Lys Ala
             85
                               90
                                                   95
Thr Ile Val Leu Ser Ile Met His Leu Ser Gly Ile Lys Asp Ile Ser
                   105
          100
                                               110
Lys Phe Ala Met His Tyr Ile Ile Glu Glu Ile Asp Glu Asp Thr Ser
115 120 125
Met Glu Asp Leu Gln Lys Met Met Ile Val Ala Leu Ile Tyr Arg Leu
                    135
                                      140
 130
Leu Val Cys Phe Tyr Glu Ile Ile Cys Ile Trp Gly Ala Gly Gly Ala
                150
                                 155
145
Thr Pro Gly Lys Phe Leu Leu Gly Leu Arg Val Val Thr Cys Asp Thr
             165
                               170
                                                  175
Ser Val Leu Ile Ala Pro Ser Arg Val Leu Val Ile Pro Ser Ser Asn
         180
                             185
                                               190
Val Ser Ile Thr Thr Ser Thr Ile Arg Ala Leu Ile Lys Asn Phe Ser
                200
                                          205
Ile Ala Ser Phe Phe Pro Ala Phe Ile Thr Leu Leu Phe Phe Gln His
               215
                                       220
Asn Arg Thr Ala Tyr Asp Ile Val Ala Gly Thr Ile Val Val Lys Arg
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Asn Gly Val Arg
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<210> 655

<211> 265

<212> PRT

<213> Rat

<400> 655

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Leu Glu Leu Arg Gly Val Val Phe Pro Tyr Gln Pro Arg Glu Gly Arg
              165
                                170
                                                 175
Tyr Gln Leu Asn Phe His Glu Ala Gln Gln Val Cys Gln Glu Gln Asp
          180
                           185
Ala Val Val Ala Thr Phe Glu Gln Leu Phe Arg Ala Trp Glu Glu Gly
     195 200
                                        205
Leu Asp Trp Cys Asn Ala Gly Trp Leu Gln Asp Ala Ser Ser Cys Arg 210 215 220
Phe Gly Thr Ser Ser Cys Arg Ile Arg His Glu Ala Cys Arg Pro
       230 235
Leu Trp Cys Gly Asp Pro Arg Val Asn Pro Pro Thr Pro Cys Leu Thr
             245
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Arg Arg Gln Asn Leu Gln Leu Arg Thr
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<211> 343
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<213> Rat
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Met Ala Val Cys Pro Tyr Gly Ala Ala Ala Val Val Met Ala Leu Leu
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Ser Ala Ala Ile Ala Phe His Trp Ser Pro Leu Leu Ala Val Leu Gln
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Arg Ala Leu Ser Leu His Thr Ala His Ala Thr Lys Asp Met Asp Asn
     35
                        40
Leu Phe Gln Leu Val Arg Asn Ile Val Pro Ala Leu Thr Ser Lys Lys
                    55
  50
                                      60
His Lys Gly Gln Asp Gly Arg Ile Gly Ile Val Gly Gly Cys Gln Glu
         70
                                  75
Tyr Thr Gly Ala Pro Tyr Phe Ala Gly Ile Ser Ala Leu Lys Val Gly
           . 85
                               90
                                                 95
Ala Asp Leu Thr His Val Phe Cys Ala Arg Glu Ala Ala Pro Val Ile
        100
                          105 . 110
Lys Ser Tyr Ser Pro Glu Leu Ile Val His Pro Val Leu Asp Ser Ser 115 120 125
Asp Ala Val Glu Val Lys Lys Trp Leu Pro Arg Leu His Ala Leu
  130
              135 140
Val Val Gly Pro Gly Leu Gly Arg Asp Asp Leu Leu Leu Asn Asn Val
                 150
                                   155
Arg Gly Ile Leu Glu Ser Thr Lys Ala Arg Asp Ile Pro Val Val Ile
             165
                              170
                                                175
Asp Ala Asp Gly Leu Trp Leu Ile Ala Gln Arg Pro Ala Leu Val His
         180
                  185
                                             190
Gly Tyr Gln Lys Ala Val Leu Thr Pro Asn His Val Glu Phe Ser Arg
     195
                      200
                                          205.
Leu Trp Asp Ala Val Leu Ser Ser Pro Met Asp Thr Ser Asn His Ser
          215
                              220
Gly Ser Val Leu Lys Leu Ser Gln Ala Leu Gly Asn Ile Thr Ile Val 225 230 235 240
Gln Lys Gly Glu Gln Asp Leu Ile Ser Asn Gly Gln Gln Val Leu Val
             245
                      250
Cys Asn Gln Glu Gly Ser Ser Arg Arg Cys Gly Gly Gln Gly Asp Leu
         260
                           265
                                            270
Leu Ser Gly Ser Leu Gly Val Met Ala His Trp Ala Leu Arg Ala Gly
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280

285

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Pro Glu Lys Thr Asn Gly Ser Ser Pro Leu Leu Val Ala Ala Trp Gly
                    295
  290
                                       300
Ala Cys Thr Leu Thr Arg Glu Cys Asn His Leu Ala Phe Gln Lys Tyr
                  310
                                   315
                                                       320
Gly Arg Ser Thr Thr Thr Thr Asp Met Ile Ala Glu Val Gly Ala Ala
             325
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Phe Ser Lys Leu Phe Thr Thr
           340
<210> 657
<211> 61
<212> PRT
<213> Rat
<400> 657
Met Pro Cys Trp Ser Leu Tyr Gln Leu Met Val Leu Tyr Gln Ile Ile
               5
                                10
Ile Leu Phe Phe Leu Phe Lys Gln Val Ser Val Arg Thr Cys Tyr Leu
    20
                             25
                                              30
Ser Thr Glu Gly Lys Pro Cys Gly Ser Val Leu Phe Ala Cys Lys Ser
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                        40
                                     45
L'eu Gln Gln Cys Leu Leu Thr Val Leu Val Thr Pro Val
                      55
  50
<210> 658
<211> 1172
<212> PRT
<213> Rat
<400> 658
Met Leu Trp Ala Leu Ala Leu Leu Ala Leu Gly Ile Gly Pro Arg Ala
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                                 10
                                                   15
Tyr Ala Gly Asp His Gly Glu Asp Thr Ala Phe Asp Leu Phe Ser Ile
          20
                            25
                                               30
Ser Asn Ile Asn Arg Lys Thr Ile Gly Ala Lys Gln Phe Arg Gly Pro
     35
                         40
                                            45
Asp Pro Gly Val Pro Ala Tyr Arg Phe Val Arg Phe Asp Tyr Val Pro
 · 50
                    55
Pro Val Asn Thr Asp Asp Leu Asn Arg Ile Val Lys Leu Ala Arg Arg
                  70
                                    75
Lys Glu Gly Phe Phe Leu Thr Ala Gln Leu Lys Gln Asp Arg Lys Ser
                                90
              85
                                                   95
Arg Gly Thr Leu Leu Val Leu Glu Gly Pro Gly Thr Ser Gln Arg Gln
         100 105
                                     . 110
Phe Glu Ile Val Ser Asn Gly Pro Gly Asp Thr Leu Asp Leu Asn Tyr
      115
                         120
                                            125
Trp Val Glu Gly His Gln His Thr Asn Phe Leu Glu Asp. Val Gly Leu
                  135
                                       140
Ala Asp Ser Gln Trp Lys Asn Val Thr Val Gln Val Ala Ser Asp Thr
                  150
                                    155
                                                       160
Tyr Ser Leu Tyr Val Gly Cys Asp Leu Ile Asp Ser Val Thr Leu Glu
              165
                               170
Glu Pro Phe Tyr Glu Gln Leu Glu Ala Asp Lys Ser Arg Met Tyr Val
         180
                      185
                                               190
Ala Lys Gly Ala Ser Arg Glu Ser His Phe Arg Gly Leu Leu Gln Asn
       195
                         200
                                            205
Val His Leu Val Phe Ala Asp Ser Val Glu Asp Ile Leu Ser Lys Lys
```

													•		
	210					215					220				
Gly 225	CÃ2	Gln	His	Ser	Gln 230	Gly	Ala	Glu	Val	Asn 235	Thr	Ile	Ser	Glu	His 240
Thr	Glu	Thr	Leu	His 245	Leu	Ser	Pro	His	Ile 250	Thr	Thr	Asp	Leu	Val 255	Val
	Gly		260					265					270		
Leu	Ser	Asn 275	Met	Met	Asn	Glu	Leu 280	Ser	Gly	Leu	His	Val 285	Met	Val	Asn
	Leu 290		_			295	_				300				
305	Glu				310					3,15	•				320
	Gln			325					330			_		335	_
	Cys		340					345					350		
	Thr	355					360					365			-
	370					375				_	380	-		_	_
385	Pro				390					395		•			400
	Gln			405					410		•			415	
_	Pro		420			_		425	•		_	_	430	_	
	Ile Ser	435					440					445			
-	450				_	455	_				460		_		
465	Ser Glu				470					475					480
	Ser			485					490					495	
	Ile		500					505	_				510		-
	Gly	515					520					525			
	530 Arg					535	_				540				
545	Ala				550					555					560
_	Pro			565				•	570		_		_	575	•
	Cys		580					585				_	590		
	Cys	595					600					605			
	610 Tyr					615					620				
625	G1u				630	•				635	•				640
	Asn			645					650					655	
			660					665.				1	670		

```
Asp Pro Met Tyr Lys Cys Glu Cys Gln Thr Gly Tyr Ala Gly Asp Gly
                        680
                                         685
Leu Ile Cys Gly Glu Asp Ser Asp Leu Asp Gly Trp Pro Asn Ser Asn
  690
                     695
                                       700
Leu Val Cys Ala Thr Asn Ala Thr Tyr His Cys Val Lys Asp Asn Cys 705 710 715 720
Pro Lys Leu Pro Asn Ser Gly Gln Glu Asp Phe Asp Lys Asp Gly Ile
725 730 735
Gly Asp Ala Cys Asp Glu Asp Asp Asp Asp Gly Val Ser Asp Glu
          740 · 745
Lys Asp Asn Cys Pro Leu Leu Phe Asn Pro Arg Gln Leu Asp Tyr Asp
                760
      755
                                  765
Lys Asp Glu Val Gly Asp Arg Cys Asp Asn Cys Pro Tyr Val His Asn 770 780
Gln Ala Gln Ile Asp Thr Asp Asn Asn Gly Glu Gly Asp Ala Cys Ser
        790 795
Val Asp Ile Asp Gly Asp Asp Val Phe Asn Glu Arg Asp Asn Cys Pro
             805
                             810
                                         815
Tyr Val Tyr Asn Thr Asp Gln Arg Asp Thr Asp Gly Asp Gly Val Gly
         820
                   825
                                     830
Asp His Cys Asp Asn Cys Pro Leu Met His Asn Pro Asp Gln Met Asp
835 840 845
Gln Asp Asn Asp Leu Val Gly Asp Gln Cys Asp Asn Asn Glu Asp Ile
            855
Asp Asp Asp Gly His Gln Asn Asn Gln Asp Asn Cys Pro Tyr Ile Ser 865 870 875 880
Asn Ser Asn Gln Ala Asp His Asp Asn Asp Gly Lys Gly Asp Ala Cys
885 890 895
                                         895
Asp Ser Asp Asp Asp Asn Asp Gly Val Pro Asp Asp Arg Asp Asn Cys 900 905 910
Arg Leu Val Phe Asn Pro Asp Gln Lys Asp Ser Asp Gly Asp Gly Arg
915 920 925
Gly Asp Ile Cys Lys Asp Asp Phe Asp Asn Asp Asn Val Pro Asp Ile
            935 940
Asp Asp Val Cys Pro Glu Asn Asn Ala Ile Thr Glu Thr Asp Phe Arg 945 950 955 960
Asn Phe Gln Met Val Pro Leu Asp Pro Lys Gly Thr Thr Gln Ile Asp
 965 970 975
Pro Asn Trp Val Ile Arg His Gln Gly Lys Glu Leu Val Gln Thr Ala
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                    985
Asn Ser Asp Pro Gly Ile Ala Val Gly Phe Asp Glu Phe Gly Ser Val
995 1000 1005
Asp Phe Ser Gly Thr Phe Tyr Val Asn Thr Asp Arg Asp Asp Tyr 1010 1015 1020
Ala Gly Phe Val Phe Gly Tyr Gln Ser Ser Ser Arg Phe Tyr Val Val
1025 1030
                       1035 104.0
Met Trp Lys Gln Val Thr Gln Thr Tyr Trp Glu Asp Lys-Pro Ser Arg
            1045 1050 . 1055
Ala Tyr Gly Tyr Ser Gly Val Ser Leu Lys Val Val Asn Ser Thr Thr 1060 1065 1070
Gly Thr Gly Glu His Leu Arg Asn Ala Leu Trp His Thr Gly Asn Thr
      1075 1080 1085
Glu Gly Gln Val Arg Thr Leu Trp His Asp Pro Lys Asn Ile Gly Trp
  1090
           1095 1100
Lys Asp Tyr Thr Ala Tyr Arg Trp His Leu Ile His Arg Pro Lys Thr 1105 1110 1115 112
Gly Tyr Met Arg Val Leu Val His Glu Gly Lys Gln Val Met Ala Asp
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1125
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Ser Gly Pro Ile Tyr Asp Gln Thr Tyr Ala Gly Gly Arg Leu Gly Leu
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Phe Val Phe Ser Gln Glu Met Val Tyr Phe Ser Asp Leu Lys Tyr Glu
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Cys Arg Asp Ala
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Leu His Asp Arg Gln Arg Val Val His Trp Asp Leu Ser Gly Gly Pro
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Gly Ser Gln Gly Arg Arg Leu Val Asp Met Tyr Ser Ala Gly Glu Gln
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Arg Val Tyr Gln Pro Arg Asp Arg Asp Arg Leu Leu Leu Ser Pro Ser 100 105 110
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Ala Phe His Asp Gly Asn Phe Ser Leu Leu Ile Arg Ala Val Glu Arg
    115 120
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Gly Asp Glu Gly Val Tyr Thr Cys Asn Leu His His His Tyr Cys His
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Leu Tyr Glu Ser Leu Ala Val Arg Leu Glu Val Thr Asp Asp Pro Leu
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Leu Ser Arg Ala Tyr Trp Asp Gly Glu Lys Glu Val Leu Val Val Ala
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Leu Gly Ala Pro Ala Leu Met Thr Cys Val Asn Arg Glu His Leu Trp
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Thr Asp Arg His Leu Glu Glu Ala Gln Gln Val Val His Trp Asp Arg
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                                       205
Gln Leu Pro Gly Val Pro His Asp Arg Ala Asp Arg Leu Leu Asp Leu
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Tyr Ala Ser Gly Glu Arg Arg Ala Tyr Gly Pro Pro Phe Leu Arg Asp
225 230 235 240
Arg Val Ser Val Asn Thr Asn Ala Phe Ala Arg Gly Asp Phe Ser Leu
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                            250
                                       255
Arg Ile Asp Asp Leu Glu Pro Ala Asp Glu Gly Ile Tyr Ser Cys His
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Leu His His His Tyr Cys Gly Leu His Glu Arg Arg Val Phe His Leu
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                                        285
Arg Val Thr Glu Pro Val Phe Glu Pro Pro Ala Arg Ala Ser Pro Gly
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                   295
                                    300
Asn Gly Ser Gly His Asn Ser Val Pro Ser Pro Asp Pro Thr Met Ala
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                               315
Arg Gly His Ser Ile Ile Asn Val Ile Val Pro Glu Asp His Thr His
325 330 335
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Phe Phe Gln Gln Leu Gly Tyr Val Leu Ala Thr Leu Leu Leu Phe Ile
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340
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Leu Leu Leu Ile Thr Val Val Leu Ala Thr Arg His Arg His Ser Gly
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Gly Cys Lys Thr Ser Asp Arg Lys Ala Gly Lys Ser Lys Gly Lys Asp
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Val Asn Met Met Glu Phe Ala Ile Ala Thr Arg Asp Gln Ala Pro Tyr
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Arg Thr Glu Asp Ile Gln Leu Asp Tyr Lys Asn Asn Ile Leu Lys Glu
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Gln Gly Gln Leu Leu Phe Ser Cys Pro Trp Ser Cys Ile Thr Ser Thr
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His Thr Phe Ile Ala Ser Ser Thr Val Leu Pro Gly Lys Val Gln Ala
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Pro Phe Ser Arg Val Leu Gln Leu Val Arg Gly Arg Ala Ser Ser Pro
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Lys Leu Met Thr Leu Trp Gly Ala Phe Pro Pro Ala Arg Gly Asp Glu
           85
                           90
                                             95
Val Leu Gly Arg Gly Trp Asn Ile Thr Ser Val Pro Leu Pro Ser His
         100
                         105
                                     110
Ser Arg Gln Val Ala Gly Ser Ala Ser His Thr His Thr Leu Gly Ala
      115
                      120
                                       125
Ala Ser Pro Thr Pro Leu Ser Pro Gly Pro Ala Pro Leu Cys Ser Thr
130
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Met Leu Pro Gly Gln Gly Thr Gly Pro Thr Leu Pro Ser Ala Gly Thr
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Val Pro Ala Leu Pro Ser Ala Ala Thr Gly Glu Gly Trp Gly Gln Val
165 170 175
Ser Arg Gly Pro His Pro Val Arg Asp Gly Val Val His Ile Pro Trp
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                                  190
Thr Cys Thr Trp Cys Leu Met Ala Ala Pro Thr Arg Asn Thr Pro Met
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Ser Ser Ile Gly Asn Met Ser His Gly His
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Ala Ile Gly Cys Pro Gln Arg His Gln Leu Pro Ala Leu Gln Glu Ala
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Thr Ala Phe Ala Gly Val His Arg Pro Leu Gln Ile His Pro Leu Gly
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Arg Gly Leu Arg Pro Trp Glu Gln Gln Gln Arg His Cys Gly His
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Ile Trp Pro Gly Trp Glu Pro Leu Arg Ser Asp Ser Leu Ala Leu Gly
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Ser Asn Lys Ser Ile Arg Thr Pro Glu Pro Val Val Gln Thr Gly Pro
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Glu Phe His Pro Ser Thr Ser Ser Glu Gln Ser Asp Thr Pro Glu Pro
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Ser Ser Gln Gly Arg Thr Arg Arg Ser Val Arg Thr Pro Glu Ala Ser
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Val Ser Thr Thr Pro Ala Leu Gln Pro Ser Thr Ser Lys Lys Gln Pro
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Thr Pro Lys Pro Thr Ala Leu Val Thr Arg Gly Arg Thr His Lys Pro
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Ser Thr Glu Gly Leu Glu Ser Val Gly Pro Val Ala Pro Asp Phe Glu
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                    135
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Pro Pro Thr Ser Thr Asp His Leu Ala Thr Ser Lys Val Thr Gly Gln
145
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Ser Leu Thr Leu Gln Ser Ser Pro Val Ser Ala Ser Pro Val Ser Thr
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                     170
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Thr Pro Glu Leu Lys Pro Pro Val Pro Ile Ala Gln Pro Leu Thr Leu
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                          185
                                         190
Glu Pro Val Pro Gln Thr Ser His Gln Arg Arg Arg Ala Thr Gly
     195 200
                                 205
Lys Gln Gly Ser Arg Thr Ala Pro Val Gly Pro Lys Ser Tyr Ser Thr.
  210
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Pro Ala Glu Pro Glu Pro Gln Ser Ser Ala Ser Gln Ser Ser Gly Ala
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Ser Glu Ala Asp Ser Pro His Gln Lys Arg Pro Arg Arg Gln Val Thr 245 250 255
Gln Lys Thr Val Val Lys Glu Glu Asp Pro Gly Glu Ile Gln Val
         260
                           265 · 270
Lys Glu Glu Pro Gln Glu Thr Ala Ile Ser Thr Pro Gly Lys Arg Lys
    275
                     280 285
Arg Asp Pro Ala Glu Gly Glu Thr Gln Gly Asn Pro Thr Arg Ser Arg
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295

300

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Arg Thr Lys Pro Asn Gln Glu Ala Ala Ala Pro Lys Val Leu Phe Thr
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Gly Val Val Asp Ser Arg Gly Glu Arg Ala Val Leu Ala Leu Gly Gly
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Ser Leu Ala Ser Ser Val Asn Glu Ala Ser His Leu Val Thr Asp Arg
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Ile Arg Arg Thr Val Lys Phe Leu Cys Ala Val Gly Lys Gly Ile Pro 355 360 365 Ile Leu Ser Leu Asn Trp Leu Tyr Gln Ser Arg Lys Ala Gly Cys Phe
  370 375
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Leu Pro Pro Asp Asp Tyr Leu Val Thr Asp Pro Glu Glu Glu Lys Asn 385 390 395 400
                                395
Phe Ser Phe Ser Leu Arg Asp Ser Leu Ser Arg Ala Arg Glu Arg Arg
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                     410
Leu Leu Glu Asp Tyr Glu Ile His Val Thr Pro Gly Val Gln Pro Pro
        420
                   425
Pro Pro Gln Met Gly Glu Ile Ile Ser Cys Cys Gly Gly Thr Val Leu
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               440
                                      445
Pro Ser Met Pro His Ser Tyr Lys Leu His Arg Val Val Ile Thr Cys
 450 455
                            460
Thr Glu Asp Leu Pro Arg Cys Ala Ile Ala Ser Arg Leu Gly Leu Pro
      470
                       475
465
Leu Leu Ser Pro Glu Phe Leu Leu Thr Gly Val Leu Lys Gln Glu Ala
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Thr Pro Glu Ala Trp Ser Ser Pro Ile Trp Lys Cys Ser Leu Pro Lys
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Lys Lys Lys
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Leu Gln Trp Val Pro Gly Ser Asp Gly Ala Ser Pro Ile Arg Tyr Phe
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Thr Val Gln Val Arg Glu Leu Pro Gly Gly Glu Trp Gln Thr Tyr Ser
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Ser Ser Ile Ser His Glu Ala Thr Leu Cys Ala Val Glu Arg Leu Arg
      70 75
65
Pro Phe Thr Ser Tyr Lys Leu Arg Leu Lys Ala Thr Asn Asp Ile Gly
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                          90 - 95
Asp Ser Asp Phe Ser Ala Glu Thr Glu Ala Val Thr Thr Leu Gln Asp
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                       105 110
Val Pro Gly Glu Pro Pro Gly Ser Val Ser Ala Thr Pro His Thr Thr
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                              125
Ser Ser Val Leu Ile Gln Trp Gln Pro Pro Arg Asp Glu Ser Leu Asn
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Gly Leu Leu Gln Gly Tyr Arg Ile Tyr Tyr Arg Glu Leu Glu Ser Glu
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Thr Gly Leu Ser Pro Glu Pro Lys Thr Leu Lys Ser Pro Ser Ala Leu
            165
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Arg Ala Glu Leu Thr Ala Gln Ser Ser Phe Lys Thr Val Asn Ser Ser
                           185
                                            190
Ser Thr Leu Thr Thr Tyr Glu Leu Thr His Leu Lys Lys Tyr Arg Arg
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                        200
                                         205
Tyr Glu Val Ile Met Thr Ala Tyr Asn Ile Ile Gly Glu Ser Pro Ala
                   215
                                     220
Ser Val Pro Val Glu Val Phe Val Gly Glu Ala Ala Pro Ala Met Ala
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                                 235
Pro Gln Asn Ile Gln Val Thr Pro Leu Thr Ala Ser Gln Leu Glu Val
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Thr Trp Asp Pro Pro Pro Glu Ser Gln Asn Gly Asn Ile Gln Gly
         260
                           265
                                           270
Tyr Lys Val Tyr Tyr Trp Glu Ala Asp Ser Arg Asn Glu Thr Glu Lys
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                                 285
Met Lys Val Leu Phe Leu Pro Glu Pro Val Val Lys Ile Lys Asp Leu
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           295
                             300
Thr Ser His Thr Lys Tyr Leu Val Ser Ile Ser Ala Phe Asn Ala Ala
               310
                                 315
Gly Asp Gly Pro Arg Ser Asp Pro Cys Gln Gly Arg Thr His Gln Ala
            325
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Ala Pro Gly Pro Pro Ser Phe Leu Glu Phe Ser Glu Ile Thr Ser Thr
          340
                           345
                                            350
Thr Leu Asn Val Ser Trp Gly Glu Pro Ser Ala Ala Asn Gly Ile Leu
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Gln Gly Tyr Arg Val Val Tyr Glu Pro Leu Ala Pro Val Gln Gly Val 370 375 380
                               380
Ser Lys Val Val Thr Val Asp Val Lys Gly Asn Trp Gln Arg Trp Leu
       390
                                  395
Lys Val Arg Asp Leu Thr Lys Gly Val Thr Tyr Phe Phe Arg Val Gln
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                               410
Ala Arg Thr Ile Ala Tyr Gly Pro Glu Leu Gln Ala Asn Val Thr Ala
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Gly Pro Ala Glu Gly Ser Pro Gly Ser Pro Arg Asn Val Leu Val Thr
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Lys Ser Ala Ser Glu Leu Thr Leu Gln Trp Thr Glu Gly Asn Thr Gly
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Asn Thr Pro Thr Thr Gly Tyr Val Ile Glu Ala Arg Pro Ser Asp Glu
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Gly Leu Trp Asp Met Phe Ala Lys Asp Ile Pro Arg Ser Ala Thr Ser
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                               490
Tyr Thr Val Gly Leu Asp Lys Leu Arg Gln Gly Val Thr Tyr Glu Phe
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Arg Val Val Ala Val Asn Lys Ala Gly Phe Gly Glu Pro Ser Arg Pro
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Ser Ile Ala Val Ser Ala Gln Ala Glu Ala Pro Phe Tyr Glu Glu Trp
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Trp Phe Leu Leu Val Ile Ala Leu Ser Ser Leu Leu Leu Val Leu Leu
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Val Val Phe Val Leu Val Leu His Gly Gln Ser Lys Lys Tyr Lys Asn
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                               570
                                                 575
Cys Gly Ser Gly Lys Gly Ile Ser Asn Met Glu Glu Thr Val Thr Leu
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                           585
Asp Asn Gly Gly Phe Ala Ala Leu Glu Leu Asn Ser Arg His Leu Asn
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Val Lys Ser Thr Phe Ser Lys Lys Asn Gly Thr Arg Ser Pro Pro Arg
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                                      620
Pro Ser Pro Gly Gly Leu His Tyr Ser Asp Glu Asp Ile Cys Asn Lys
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630

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Tyr Asn Gly Ala Val Leu Thr Glu Ser Val Asn Leu Lys Glu Lys Ser
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Val Asp Gly Ser Glu Ser Glu Ala Ser Asp Ser Asp Tyr Glu Glu Ala
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               665 . 670
Leu Pro Lys His Ser Phe Val Asn His Tyr Met Ser Asp Pro Thr Tyr 675 680 685
675 680 685
Tyr Asn Phe Trp Lys Arg Arg Pro Pro Ala Ala Ala Pro His Arg Tyr
                  695
Glu Ala Val Ala Gly Ala Glu Ala Gly Pro His Leu His Thr Val Ile
705
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Thr Thr Gln Ser Ala Gly Gly Val Tyr Thr Pro Ala Gly Pro Gly Ala 725 730 735
Arg Ala Pro Leu Thr Gly Phe Ser Ser Phe Val
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Val Gly Ser Asp Val Glu Leu Arg Cys Val Tyr Pro Arg Arg Ser His
35 40 45
Phe Ser Leu Asp Asp Leu Tyr Val Tyr Trp Gln Ile Val Asp Glu Ala 50 55 60
Lys Thr Val Val Thr Tyr Tyr Leu Pro Ser Ala Asn Glu Ser Ser Thr
                70
                                  75
Ile His Val Ser Asn Ser Tyr Lys Asn Arg Ala His Leu Ser Pro Asp
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Leu Met Lys Glu Gly Asp Phe Ser Leu His Leu Gln Asn Val Thr Pro
100 105 110
Gln Asp Thr Gln Glu Phe Lys Cys Leu Val Phe Arg Met Ser Thr Val
 115 120 125
Leu Gly Lys Ala Leu Glu Glu Val Val Arg Leu Arg Val Ala Ala Asn
130 135 140
Phe Ser Thr Pro Val Ile Ser Thr Ser Gly Ser Ser Asp Pro Gly Gln 145 150 155 160
Glu Arg Thr Phe Thr Cys Met Ser Lys Asn Gly Tyr Pro Glu Pro Asn
            165 170
                                                   1.75
Leu Tyr Trp Ile Asn Arg Thr Asp Asn Thr Leu Ile Asp Glu Thr Leu 180 185 190
Gln Asn Asn Thr Val Tyr Leu Asn Glu Leu Gly Leu Tyr. Asp Val Val
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Ser Thr Leu Arg Ile Pro Trp Thr Pro His Val Asp Val Ile Cys Cys 210 215 220
Val Glu Asn Val Ala Leu His Gln Asn Ile Thr Ser Ile Ser Arg Ala
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                                   235
Asp Ser Phe Thr Gly Ser Met Asn Thr Glu Arg Pro Gln Glu Ile His
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Arg Glu Ala Thr Lys Val Leu Phe Tyr Ala Leu Ala Ala Leu Leu Ala 260 265 270
Val Val Val Ile Phe Ile Ile Val Leu Tyr Arg Cys Arg Arg Arg
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Pro Cys Gln Ser Tyr Thr Gly Pro Arg Ala Val Gln Leu Glu Leu Thr
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Asp His Ser
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Thr Val Asn Ala Leu His Pro Gly Val Ala Arg Thr Glu Leu Gly Arg
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His Thr Gly Met His Asn Ser Ala Phe Ser Gly Phe Met Leu Gly Pro
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Phe Phe Trp Leu Leu Phe Lys Ser Pro Gln Leu Ala Ala Gln Pro Ser 65 70 75 80
65
              70
                                75
Thr Tyr Leu Ala Val Ala Glu Glu Leu Glu Ser Val Ser Gly Lys Tyr
    85 90
Phe Asp Gly Leu Arg Glu Lys Ala Pro Ser Pro Glu Ala Glu Asp Glu
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Glu Val Ala Arg Arg Leu Trp Thr Glu Ser Ala His Leu Val Gly Leu
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Asp Met Ala His Gly Ser Ser Gly Arg Gly His Ser Ile Ser Arg
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Arg Lys Ser Glu Glu Pro Ala Val Arg Lys Lys Glu Ser Ser Leu Arg
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                                        45
Thr Lys Ile Arg Glu Leu Arg Gln Gln Arg Asp Lys Leu Arg Ala Glu
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Val Lys Gln Trp Gly Ala Arg Val Lys Glu Pro Pro Ala Lys Glu Asp
65 1
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                                  75 . 80
Pro Ser Arg Thr Val Ile Ser Glu Gln Glu Val Leu Glu Arg Glu Trp
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Arg Asn Val Asp Ala Ile Leu Glu Ala Tyr Arg Phe Thr Gly Leu Ser 100 105 110
Gly Lys Leu Thr Ser Arg Gly Val Cys Met Cys Ile Ser Thr Ala Phe
      115
                      120
                              · 125
Glu Gly Asn Leu Leu Asp Ser Tyr Phe Val Asp Leu Val Ile Glu Lys
 130
               135
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Pro Leu Arg Ile His His Ser Val Pro Val Phe Ile Pro Leu Glu
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Lys Ile Ala Ala Ala His Leu Gln Thr Asp Val Gln Arg Phe Leu Phe
              165
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Arg Leu Trp Glu Tyr Leu Asn Ala Tyr Ala Gly Arg Lys Tyr Gln Ala
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                        185
Asp Gln Leu Glu Ser Asp Phe Cys Asp Val Leu Thr Gly Pro Leu Gln
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                     200
                                        205
Arg Asn Ala Leu Cys Asn Leu Leu Ser Phe Thr Tyr Lys Val Glu Gln
210 215 220
                  215
                                     220
Arg Cys Gln Thr Phe Ser Phe Ser Ala Arg Leu Leu Tyr Glu Asp Pro
225 230 235
                                                    240
Thr Ala Ala Leu Pro Thr Asn Val Thr Val Thr Arg Pro Gly Val Glu
            245
                              250
                                                 255
Ala Ser Ser Pro Pro Trp Glu Glu His Arg Ala Ser His Gln Met Leu
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Phe Arg Thr Lys Pro Leu His Lys Val Phe Ala Ser Phe Ser Lys Glu 275 280 285
Thr Glu Lys Leu His Leu Asn Leu Val Ser
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Leu Leu Arg Trp His Asp Gly His Gln Phe Cys Ser Lys Ser Gly Gln
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Pro Thr Gln Lys Asn Val Ala Gly Ser Lys Arg Val Cys Pro Ser Ser
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Lys Ile Ile Tyr Tyr Pro Gln Met Ala Pro Val Val Ile Thr Leu Val
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Ser Asp Gly Ala Arg Cys Leu Leu Ala Arg Gln Ser Ser Phe Pro Lys
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Gly Leu Tyr Ser Ala Leu Ala Gly Phe Cys Asp Ile Gly Glu Ser Val
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Glu Glu Thr Val His Arg Glu Val Ala Glu Glu Val Gly Leu Glu Val
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                                         125
Glu Asn Ile Gln Tyr Ser Ala Ser Gln His Trp Pro Phe Pro Asn Ser
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Ser Leu Met Ile Ala Cys His Ala Thr Val Lys Pro Gly His Thr Glu
145 150 155
Ile Gln Val Asn Leu Lys Glu Leu Glu Ala Ala Trp Phe Ser Leu
            165
                             170 175
Asp Glu Val Thr Thr Ala Leu Arg Arg Lys Gly Ser Leu Ala Leu Gln
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                                   190
Pro Ser Glu Ala Ser Pro Leu Leu Pro Pro Lys Leu Ala Ile Ala
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                                        205
His His Leu Ile Lys Lys Trp Val Glu Thr Arg Ser Cys Ser Ser Leu
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Ala Ala
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Ala Ile His Val Leu Ser Gly Val Trp Val Ala Tyr Glu Arg Val Gly
         420
                          425
                                            430
Phe Ser Gly Glu Gln Tyr Ile Leu Glu Lys Gly Val Tyr Arg Asn Cys
       435
                        440
                                       445
Asp Asp Trp Gly Ser Gly Asn Cys Ala Leu Gly Ser Leu Gln Pro Val
                   455
                                      460
Val Gln Val Gly Glu Ser Asp Leu His Phe Val Thr Lys Ile Gln Leu
465
                470
                                  475
Phe Ser Gly Pro Asn Phe Leu Gly Asp His Ile Ser Phe Glu Asp Asp
           485
                              490
Gln Ala Ser Leu Pro Ala Ser Phe His Pro Gln Ser Cys Arg Val His
                 505
         500
                                            510
Gly Gly Ser Trp Val Leu Phe Glu Asp Lys Asn Phe Glu Ala Asp Gln
               520
      515
                                        525
His Ile Val Ser Glu Gly Glu Phe Pro Thr Leu Thr Asp Met Gly Cys
 530 535
                                    540
Leu Ala Ser Thr Val Leu Gly Ser Leu Arg Lys Val Pro Leu His Phe
545
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                         555
Ser Glu Pro Ser Leu Ser Leu Phe Gly Leu Glu Cys Phe Glu Gly Lys
                      . 570
           565
                                               575
Glu Ile Glu Leu Thr Gly Glu Val Arg Ser Leu Gln Ala Glu Gly Phe
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                        585
                                            590
Asn Asn His Val Leu Ser Val Arg Val Lys Gly Gly Val Trp Val Val
      595
                      600
                                       605
Cys Glu His Ser Asp Phe Arg Gly Arg Gln Trp Leu Val Gly Ser Cys
  610
           615
                                      620
Glu Ile Thr Asn Trp Leu Thr Tyr Ser Gly Thr Gln Arg Val Gly Ser 625 630 635 640
Leu Tyr Pro Ile Lys Gln Arg Arg Ala Tyr Phe Arg Leu Trp Asn Ala
            645
                              650
Ala Leu Gly Gly Phe Leu Ser Val Pro Asp His Val Glu Asp Met Lys
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                  665
                                            670
Ala Gly Arg Val Val Ser Glu Pro Arg Ala Gly Gly Ser Cys Ile
      675
               680
                                         685
Trp Tyr Tyr Glu Asp Gly Leu Leu Lys Asn Gln Met Ala Pro Thr Met 690 695 700
Ser Leu Gln Val Ile Gly Pro Pro Ser Pro Gly Ser Lys Val Val Leu
              710 715
Trp Ala Glu Ser Arg Leu Pro Arg Gln Thr Trp Ser Ile Asn Glu Leu
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                              730
                                          735
Gly His Ile Cys Ser Gln Met Phe Glu Gly Gln Ile Leu Asp Val Lys
                  745
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Gly Gly Arg Gly Tyr Asp Arg Asp His Val Val Leu Trp Glu Pro Thr 755 760 765
Lys Asp Arg Leu Ser Gln Ile Trp Thr Val His Val Leu
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                         10 15
Gln Leu Gly Glu Leu Asn Arg Thr Ala Val Phe Thr Cys Arg Pro Ala
                            25,
```

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Arg Val Lys Glu Gly Asp Ile Leu Tyr Ile His Ser Leu Gln Thr Val
    . 35
                       40
                                        45
Gly Ser Asn His Lys Pro Val Ala Ala Glu His Thr Tyr Trp Ala Trp
  50
                    55
Pro Glu Glu Thr Asp Val
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<213> Mouse
<400> 670
Leu Thr Asn Gly Ser Gln Ala Ser Asp Lys Ser Glu Glu Gly Ser Ala
1
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Asp Thr Ala Asp Pro Gln Glu Asn Pro Leu Gln Pro Val Ser Val Gly
        20
                           25
Glu Glu Pro Ser Ile Thr Glu His His Ser Val Gly Glu Gln Ala Trp
      35
                      40
Asp Gly Thr Ser Gln Ser Cys Pro Ser Leu Pro Ala Thr Val Ser Phe 50 55 60
His Met Asp Ser Thr Asp Leu Glu Pro Gly Gln Gln Thr Ala Met Lys
             7.0
65
                     75
Ser Cys Ser Arg Asp Asp Val Glu Met Val Glu Glu Phe Asp Glu Leu
            85 90
                                                95
Pro Thr Asp Ala Val Arg Arg Ile Arg Arg Glu Leu Val Thr Val Thr
                          105
                                      110
         100
Lys His Ser Pro Glu Gln Arg Gln Asp Pro Leu Cys Ile Ser Ile Thr
               120
    115
                                        125
Val Cys Thr Val Glu Lys Asp Arg Pro Ala Ala Leu Asp Ser Leu Glu
  130 135
                             140
Glu Pro Leu Pro Gly Met Leu Phe Phe Leu Ser Ser Gly Gln Asp Gln
                150
                                  155
                                                     160
Gln Ala His Pro Gln Leu Arg Glu His Pro Ala Pro Glu Ala Ser Glu
          165
                  170
Ala Ser Gln Pro Gln Asp Ala Ala Glu Gly Ser Ser Ala Gly Glu Glu 180 185 . 190
Lys Asp Ala Ser Val Glu Pro Leu Leu Pro Ala Ala Ser Pro Gly Gly
      195
                       200
                                        205
Ser Thr Ser Gln Val Leu Glu Ala Ala Thr Cys Lys Lys Gln Val Ser
 210
                                     220
                  215
Gln Asp Phe Leu Glu Thr Arg Phe Lys Ile Gln Gln Leu Leu Glu Pro
225
                230
                                  235
Gln Gln Tyr Met Ala Cys Leu Pro His His Ile Ile Val Lys Ile Phe
           245 250
Arg Leu Leu Pro Thr Leu Ser Leu Ala Ile Leu Lys Cys Thr Cys Arg
         260
                         265
                                           . .270
Tyr Phe Lys Ser Ile Ile Glu Tyr Tyr Asn Ile Arg Pro Ala Asp Ser
                      280
Arg Trp Val Arg Asp Pro Arg Tyr Arg Glu Asp Pro Cys Lys Gln Cys 290 295 300
Lys Lys Lys Tyr Val Lys Gly Asp Val Ser Leu Cys Arg Trp His Pro
305
             310
                            315
Lys Pro Tyr Cys Gln Ala Leu Pro Tyr Gly Pro Gly Tyr Trp Met Cys
            · 325
                              330 335
Cys Pro Pro Val Ser Glu Gly Leu Phe Cys Cys Lys Leu Gly Leu His
          340
                            345
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Asp Asn His Trp Leu Pro Ala Cys His Ser Phe Asn Pro Gly Asn Pro
                        360
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Thr His Phe Ile His Thr Leu Thr Arg Leu Gln Met Glu Gln Gly Ala
              5
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1
                                              15
Glu Ser Leu Gly Asp Leu Glu Ser Pro Val Glu Asp Thr Pro Val Glu
       20
                       25
Gln Ala Ala Leu Ser Pro Phe Pro Pro Ser Lys Pro Pro Val Ser Ser
     35 40
Glu Leu Gly Asp Ser Ser Cys Ser Ser Asp Met Thr Asp Ser Ser Thr
 50 55
                                   60
Thr Leu Ser Ser Gly Ser Ser Glu Pro Pro Asn His Pro Ala His Pro 65 70 75 80
Ser Leu Pro Gly Pro Ser Phe Arg Ser Gly Val Asp Glu Asp Ser Leu 85 90 95
Glu Gln Ile Leu Asn Phe Ser Asp Ser Asp Leu Gly Ile Glu Glu
        100
                       105
                                         110
Glu Glu Glu Gly Gly Val Gly Asn Ser Asp Asn Leu Ser Cys Phe
    115
                      120
                               125
His Leu Ala Asp Ile Phe Gly Thr Gly Asp Pro Gly Ser Leu Ala Ser
 130 135 140
Trp Thr His Ser Gln Ser Gly Ser Ser Leu Ala Ser Gly Ile Leu Asp
145 150 150 155 160
                        155
               150
                                                160
Glu Asn Ala Asn Leu Asp Ala Ser Cys Phe Leu Asn Ser Gly Leu Gly
                             170
            165
                                             175 -
Gly Leu Arg Glu Gly Ser Leu Pro Gly Ser Ser Gly Ser Pro Glu Gly
         180
                         185
                                            190
Asp Ala Val Gln Ser Ser Ser Trp Asp Leu Ser Leu Ser Ser Cys Asp 195 200 205
Ser Phe Glu Leu Leu Gln Ala Leu Pro Asp Tyr Ser Leu Gly Pro His
 210 215 220
Tyr Thr Ser Arg Arg Val Ser Gly Ser Pro Asp Ser Leu Glu Thr Phe
225 230 235
His Pro Leu Pro Ser Phe Ser Pro Pro Arg Asp Ala Ser Thr Cys Phe
        245 250 255
Leu Glu Ser Leu Val Gly Leu Ser Glu Pro Val Thr Glu Val Leu Ala
                  265
         260
                                          270
Pro Leu Leu Glu Ser Gln Phe Glu Asp Ala Ala Leu Ala Pro Leu Leu
     275
                      280
                                        285
Glu Pro Val Pro Val
  290
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Met Glu Val Asn Cys Leu Thr Leu Lys Asp Leu Ile Ser Pro Arg Gln
              5
                            10
Thr Arg Leu Asp Phe Ala Ile Glu Asp Ala Glu Asn Ala Gln Lys Glu
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20
                             25
Asn Ile Phe Val Asp Arg Ser Arg Met Thr Pro Lys Thr Pro Met Lys
      35
                         40
Asn Glu Pro Ile Asp Leu Ser Lys Gln Arg Ile Phe Thr Pro Asp Arg
 50
                     55
Asn Pro Ile Thr Pro Val Lys Pro Val Asp Arg Gln Pro Gln Val Glu
65 70 75 80
Pro Trp Thr Pro Thr Ala Asn'Leu Lys Met Leu Ile Ser Ala Ala Ser
           85
                               90
Pro Asp Ile Arg Asp Arg Glu Lys Lys Lys Glu Leu Phe Arg Pro Ile
         100
                            105
                                               110
Glu Asn Lys Glu Asp Ala Phe Val Asn Ser Leu Gln Leu Asp Val Ala
     115
                       120
Gly Asp Gly Ala Val Asp Glu Tyr Glu Lys Gln Arg Pro Ser Arg Lys
130 135 140
Gln Lys Ser Leu Gly Leu Leu Cys Gln Lys Phe Leu Ala Arg Tyr Pro
       150
                                  155
Ser Tyr Pro Leu Ser Thr Glu Lys Thr Thr Ile Ser Leu Asp Glu Val
            165
                              170
                                                  175
Ala Val Ser Leu Gly Val Glu Arg Arg Arg Ile Tyr Asp Ile Val Asn
180 185 190
                            185
                                            190
Val Leu Glu Ser Leu His Leu Val Ser Arg Val Ala Lys Asn Gln Tyr
  195
               200
                                         205
Gly Trp His Gly Arg His Ser Leu Pro Lys Thr Leu Arg Thr Leu Gln
  210
                     215
                                       220
Arg Leu Gly Glu Glu Gln Lys Tyr Glu Glu Gln Met Ala Cys Leu Gln
               230
                            235
Gln Lys Glu Leu Asp Leu Met Gly Tyr Arg Phe Gly Glu Arg Arg Lys
245 250 255
Asp Gly Ser Pro Asp Pro Arg Asp Pro His Leu Leu Asp Phe Ser Glu
         260
                   265 270
Ala Asp Tyr Pro Ser Ser Ala Asn Ser Arg Lys Asp Lys Ser Leu
               280
      275
                                          285
Arg Ile Met Ser Gln Lys Phe Val Met Leu Phe Leu Val Ser Lys Thr
290 295 300
Lys Ile Val Thr Leu Asp Val Ala Ala Lys Ile Leu Ile Glu Glu Ser
305 310 315
Gln Asp Thr Pro Asp His Ser Lys Phe Lys Thr Lys Val Arg Arg Leu
             325
                               330
                                                   335
Tyr Asp Ile Ala Asn Val Leu Thr Ser Leu Ala Leu Ile Lys Lys Val
         340
                       345
                                      350
His Val Thr Glu Glu Arg Gly Arg Lys Pro Ala Phe Lys Trp Ile Gly
355 360 365
       355
                         360
                                           365
Pro Val Asp Phe Ser Ser Ile Asp Glu Glu Leu Leu Asp Val Ser Ala
  370
                     375
                                       380
Ser Ile Leu Pro Glu Leu Lys Lys Glu Ala Tyr Gly Gln Ile Arg Vaļ
                 390
                                    395
Cys Ala Lys Glu Arg Leu Val Arg Tyr Gly Ser Phe Asn Thr Val His
405 410 415
             405
                                410
                                                  415
Thr Ser Glu Lys Ile Gln Arg Lys Val Ser Ser Glu Pro Ser Ser Pro
         420
                           425
                                            430
Gln Gly Glu Arg Gln Gly Ser Ala Tyr Ser Leu Glu Ile Gly Ser Leu
      435
                         440
                                 . 445
Ala Ala Ile Tyr Arg Gln Lys Val Glu Asp Asn Ser Gln Glu Glu Ala
                    455
                                  460
Phe Val Ser Asn Thr Ala Val Pro Pro Ala Ser Ile Leu Asp Pro Ala
                             , 475
                  470
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Leu Ser Met Asp Ser Glu Tyr Cys Val Lys Pro Leu Ala Gln Pro Val
               485
                                490
Phe Ser Val Ala Gln Thr Asp Leu Pro Ala Phe Ser Ala Gln Asn Gly
                                               510
          500
                            505
Pro Ser Gly Gln Val Gly Val Pro Val Pro Ser Ala Ala Ser Asp Thr
                     520
       515
                                           525
Glu Asn Leu Lys Pro Ala Leu Leu Ala Gly Gln Pro Leu Val Tyr Val
                    535`
                                       540
Pro Ser Thr Gln Leu Phe Met Leu Tyr Gly Ser Val Gln Glu Gly Leu
           . 550
                                    555
Ser Pro Glu Ser Arg Ser Glu Glu Asp Gly Gly Gly Ser Asp Val Pro
565 570 575
              565
Ala Asp Leu Ser Val Thr Pro Ser Ala Gln Lys Arg Leu Cys Glu Glu
                   585
         580
                                            590
Arg Asp Pro Gln Glu Glu Glu Asp Glu Pro Ala Met Lys Arg Gln Ser
      595
                        600
                                           605
Gln Glu Phe Glu Asp Ser Pro Leu Ser Leu Val Met Pro Lys Lys Pro
                   615
 610
                                       620
Ser Ser Ser Thr Asp Leu Ala Cys Pro Val Thr Met Gly Asn Gly Ser
                 630
                                  635
                                                       640
Ser Pro Pro Leu Glu Asp Ala Cys Val Lys Gly Gln Leu Pro Ala Ala
             645
                              650
                                                  655
Glu Glu Val Thr Gly Lys Ala Ala Pro Asn Cys Tyr Val Ala Ser Glu
           660
                             665
                                               670
Cys Gly Asn Pro Ala Arg Asn Pro Asp Thr Glu Lys Pro Ser Asn Glu
      675
                        680
                                         685
Asn Glu Ile Thr Lys Asp Pro Ser Leu Met Gln Tyr Leu Tyr Val Gln
  690
                    695
                                        700
Ser Pro Ala Gly Leu Asn Gly Phe Asn Met Val Leu Pro Gly Thr Gln
705
               710
                         715
Thr Pro His Thr Val Ala Pro Ser Pro Ala Gln Leu Pro Ser Phe Gly
            725
                               730
                                                   735
Val Pro Cys Met Phe Leu Gln Ser Pro Gly Leu Gly Pro Phe Pro Val
          740
                    745
                                        750
Leu Tyr Ser Pro Ala Ile Pro Gly Pro Ile Ser Ser Ala Pro Gly Thr
     755
               760
                                 765
His Pro Asn Pro Gly Pro Met Asn Phe Gly Leu Ser Thr Leu Ala Ser
                     775
                                       780
Ala Ser His Leu Leu Ile Ser Pro Ala Ala Met Val Asn Pro Lys Pro
                790
                                    795
Ser Thr Leu Pro Cys Thr Asp Pro Gln Leu Arg Cys Gln Pro Ser Leu 805 810 815
Asn Leu Asn Pro Val Met Pro Gly Ser His Gly Val Ile His Pro Glu
          820
                            825
                                                830
Ser Pro Cys Tyr Val Arg His Pro Val Ser Met Val Lys Ala Glu Gln
835 840 845 .
Ser Pro Ala Pro Ala Thr Pro Lys Ser Ile Gln Arg Arg His Arg Glu
850 855 860
Thr Phe Phe Lys Thr Pro Gly Ser Leu Gly Asp Pro Val Phe Arg Arg
                870
                                    875
Lys Glu Arg Asn Gln Ser Arg Asn Thr Ser Ser Ala Gln Arg Arg Leu
              885
                                 890
Glu Ile Ser Ser Ser Gly Pro Asp
          900
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<212> PRT <213> Mouse <400> 673 Lys Arg Arg Lys Arg Lys Arg Ser Glu Gly Leu Ser Gln Glu Ala Thr 10 Pro Ser Gln Asp Leu Ile Gln His Ser Cys Ser Pro Val Asp His Ser 20 25 30 Glu Pro Glu Ala Arg Thr Glu Leu Gln Lys Lys Lys Lys Lys Arg 35 . 40 45 Arg Lys Arg Lys Pro Glu Pro Gln Gln Asp Glu Glu Ser Lys His Pro 50 55 Gly Asp Gln Arg Ser Pro Arg Pro Ser Val Thr Pro Val Pro Ala Leu 65 70 75 80 Ser Val Asn Gly His Leu Pro Ser Asp Cys Leu Val Leu Thr Trp Asp . 85 90 Gly Glu Pro Ser Ala Ile Ser Gln Asp Ala Ile Lys Asp Ser Arg Leu 100 105 110 Ala Arg Thr Gln Thr Val Val Asp Asp Trp Asp Glu Glu Phe Asp Arg 115 120 125 Gly Lys Glu Lys Lys Ile Lys Lys Phe Lys Arg Glu Lys Lys Arg Asn 130 135 140 Phe Asn Ala Phe Gln Lys Leu Gln Ser Arg Arg Asn Phe Trp Ser Val 145 150 155 Thr His Pro Ala Lys Val Ala Ser Leu Ser Tyr Arg Arg 165 170 <210> 674 <211> 470 <212> PRT <213> Mouse <400> 674 Glu Glu Thr Lys Pro Leu Leu Gly Ser Asp Val Ser Gly Pro Glu Gly 10 Thr Lys Val Met Gly Ala Val Pro Cys Arg Arg Ala Leu Leu Cys 20 25 Asn Gly Met Arg Tyr Lys Leu Leu Gln Glu Gly Asp Ile Gln Val Cys 35 40 45 Val Ile Arg His Pro Arg Thr Phe Leu Ser Lys Ile Leu Thr Ser Lys 55 50 60 Phe Leu Arg Arg Trp Glu Pro His His Leu Thr Leu Ala Asp Asn Ser 70 65 75 Leu Ala Ser Ala Thr Pro Ser Gly Tyr Met Glu Asn Ser Val Ser Tyr 85 90 95 Ser Ala Ile Glu Asp Val Gln Pro Leu Ser Trp Glu Asn Ala Pro Lys 100 105 _.110 Tyr Cys Leu Gln Leu Thr Ile Pro Gly Gly Thr Val Leu Leu Gln Ala 115 120 125 Ala Asn Ser Tyr Leu Arg Asp Gln Trp Phe His Ser Leu Gln Trp Lys 130 135 140 Lys Lys Ile Tyr Lys Tyr Lys Lys Val Leu Ser Asn Pro Ser Arg Trp 145 150 150 155 160 155 ·

Glu Val Val Leu Lys Glu Ile Arg Thr Leu Val Asp Met Ala Leu Thr

Ser Pro Leu Gln Asp Asp Ser Ile Asn Gln Ala Pro Leu Glu Ile Val

185 .

165

180

170 175

```
Ser Lys Leu Leu Ser Glu Asn Thr Asn Leu Thr Thr Gln Glu His Glu
      195
                       200
Asn Ile Ile Val Ala Ile Ala Pro Leu Leu Glu Asn Asn His Pro Pro
 210
                    215
                                      220
Pro Asp Leu Cys Glu Phe Phe Cys Lys His Cys Arg Glu Arg Pro Arg
                 230
                                235
Ser Met Val Val Ile Glu Val Phe Thr Pro Val Val Gln Arg Ile Leu 245 250 255
Lys His Asn Met Asp Phe Gly Lys Cys Pro Arg Leu Arg Leu Phe Thr
       260
                 265
                                             270
Gln Glu Tyr Ile Leu Ala Leu Asn Glu Leu Asn Ala Gly Met Glu Val
               280
                                 285
  275
Val Lys Lys Phe Ile Gln Ser Met His Gly Pro Thr Gly His Cys Pro
290 295 300
His Pro Arg Val Leu Pro Asn Leu Val Ala Val Cys Leu Ala Ala Ile
305 310
                                315
Tyr Ser Cys Tyr Glu Glu Phe Ile Asn Ser Arg Asp Asn Ser Pro Ser
             325
                              330
Leu Lys Glu Ile Arg Asn Gly Cys Gln Gln Pro Cys Asp Arg Lys Pro
        340
                          345
Thr Leu Pro Leu Arg Leu Leu His Pro Ser Pro Asp Leu Val Ser Gln
      355
                       360
                                         365
Glu Ala Thr Leu Ser Glu Pro Arg Leu Lys Ser Val Val Val Ala Ser
                    375
                           380
Ser Glu Val His Val Glu Val Glu Arg Thr Ser Thr Ala Lys Pro Ala
                390
                                395
Leu Thr Ala Ser Thr Gly Asn Asp Ser Glu Pro Asn Leu Ile Asp Cys 405 410 415
Leu Met Val Ser Pro Ala Cys Gly Thr Met Ser Ile Glu Leu Gly Pro
        420 425
                                       430
Gln Ala Gly Arg Thr Leu Gly Cys His Val Glu Ile Leu Lys Leu Leu
    435 440
                                        445
Ser Asp Tyr Asp Asp Trp Arg Pro Ser Leu Ala Ser Leu Leu Gln Pro
                    455
 450
Ile Pro Phe Pro Lys Glu
465
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<213> Mouse
<400> 675 ·
Phe Ala Arg Thr Leu Pro Trp Ala Ser Val Leu Arg Val Trp Asp Met
                                                 15
                               10
Phe Phe Cys Glu Gly Val Lys Ile Ile Phe Arg Val Ala Leu Val Leu
                            25
          20
Leu Arg His Thr Leu Gly Ser Val Glu Lys Leu Arg Ser Cys Gln Gly
     35
                      40
Met Tyr Glu Thr Met Glu Gln Leu Arg Asn Leu Pro Gln Gln Cys Met
  50
                   55
                               60
Gln Glu Asp Phe Leu Val His Glu Val Thr Asn Leu Pro Val Thr Glu
                                 75 · 80
             70
Ala Trp Ile Glu Arg Glu Asn Ala Ala Gln Leu Lys Lys Trp Arg Glu
            85
                          90
Thr Arg Gly Glu Leu Gln Tyr Arg Pro Ser Arg Arg Leu His Gly Ser
          100
                            105
```

```
Arg Ala Ile His Glu Glu Arg Arg Arg Gln Gln Pro Pro Leu Gly Pro
  · 115
                    120
                             125
Ser Ser Ser Leu Leu Ser Leu Pro Ser Leu Lys Ser Arg Gly Ser Arg
 130
                 135
                                   140
Ala Val Gly Gly Ala Pro Ser Pro Pro Pro Pro Val Arg Arg Ala Ser
              150
                              155
                                                 160
Ala Gly Pro Val Pro Gly Ala Val Val Ile Ala Glu Gly Leu His Pro
165 170 175
            165
                                              175
Ser Leu Pro Ser Pro Thr Gly Asn Ser Thr Pro Leu Gly Thr Ser Lys
       180 185
Glu Ile Arg Arg Gln Glu Lys Glu Arg Gln Lys Gln Glu Lys Asp Arg
 195 200
                               205
Glu Lys Glu Arg Gln Arg Gln Glu Lys Glu Arg Glu Arg Gln Glu Arg
210 215 220
Ser Gly Arg Ser Gly Lys Arg Ser Lys Arg Arg Asn Ser Arg Ser Arg 225 230 235 240
Arg Arg Ser Gly Arg Ser Trp Arg Arg Lys Ala Lys Ala Gly Asn Cys
            245
                          250 255
Pro Cys Val Glu Gly Gln Met Gly Pro Arg His Pro Met Met Val Gly
        260
                 265 270
Thr Gly Gln Gln Leu Arg Pro Gly Arg Met Leu Thr Phe Asp Leu Trp 275 280 285
Leu Asp Leu Asp Gly Met Ala Leu Leu Leu Pro Leu Ile Glu Ser Ser
 290 295 300
Pro Gly Arg Leu Ser Gln Leu Pro Leu Ala Gly Ser Ser Phe Phe
305
          310
                                 315
<210> 676
<211> 94
<212> PRT
<213> Mouse
<400> 676
Met Phe Ser Glu Lys Lys His Phe Leu His Thr Ile Gln Asn Pro Glu
20
                         25
                                        30
Arg Glu Arg Lys Lys Glu Arg Lys Lys Glu Arg Lys Glu Arg Lys
     35
                                       45
                      40
Gln Ala Ser Leu Pro Ser Val Lys Arg Glu Arg Ala Trp His Gly Glu
           55
                               60
Gln Thr Gln Gly Ser Leu Ser Thr Val Arg Gln Glu Ser Ser Pro, Gly
65
             70
                                 75
His Arg Ala Lys Val Ile Ala Asp Leu Gly Lys Asn Asp Gln
<210> 677
<211> 137
<212> PRT
<213> Mouse
Val Arg Trp Lys Met Arg Arg Ser Leu Arg Ala Gly Arg Arg Arg Gln
                            10
                                             15
Thr Ala Gly Arg Lys Ser Lys Ser Pro Pro Lys Val Pro Ile Val Ile
         20
                         25 ·
Gln Asp Asp Ser Leu Pro Thr Gly Pro Pro Pro Gln Ile Arg Ile Leu
```

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40
                                             45
Lys Arg Pro Thr Ser Asn Gly Val Val Ser Ser Pro Asn Ser Thr Ser
  50
                   55
                                        60
Arg Pro Ala Leu Pro Val. Lys Ser Leu Ala Gln Arg Glu Ala Glu Tyr
                 70
                                   75
Ala Glu Ala Arg Arg Ile Leu Gly Ser Ala Ser Pro Glu Glu Glu 85 90 95
Gln Glu Lys Pro Ile Leu Asp'Arg Pro Thr Arg Ile Ser Gln Pro Glu
         100 105 110
Asp Ser Arg Gln Pro Ser Asn Val Ile Arg Gln Pro Leu Gly Pro Asp
      115
                        120
Gly Ser Gln Gly Phe Lys Gln Arg Arg
  130
                     135
<210> 678
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Glu Thr Thr Ile Thr Thr Asp Ser Arg Asp Tyr Gln Met Ala Lys Gly
1
               5
                                 10
Lys Arg Lys Asn Leu Thr Asn Arg Asn Gln Asp His Ser Leu Ser Ser
        20
                             25
Glu Pro Ser Thr Pro Thr Ser Ala Ser Pro Gly Tyr Pro Asp Thr Pro
  35
                       40
                                            45
Glu Lys Gln Asp Ser Asn Leu Lys Ser Tyr Leu Met Met Leu Val Glu
50 55 60
Asp Ile Lys Lys Gly Phe Asn Asn Ser Leu Lys Glu Val Lys Glu Asn 65 70 75 80
Thr Ala Lys Glu Val Glu Val Leu Lys Glu Ile Gln Glu Asn Thr Thr
              85
                                90
Lys Gln Val Met Glu Leu Asn Lys Ile Ile Gln Asp Leu Lys Arg Glu
          100
                     105
                                              110
Val Glu Thr Lys Lys Thr Gln Asn Glu Thr Thr Leu Glu Ile Glu Thr
115 120 125
                        120
Leu Val Lys Lys Ser Gly Thr Ile Asp Val Ser Ile Ser Asn Arg Ile
                   135
                                       140
Gln Glu Met Glu Glu Arg Ile Ser Gly Ala Glu Asp Ser Ile Glu Asn
                 150
                                    155
Ile Gly Thr Thr Thr Lys Glu Asn Ala Lys Arg Lys Lys Ile Leu Thr
             165
                         170
Gln Asn Ile Gln Lys Ile Gln Asp Lys Met Arg Arg Pro Asn Leu Trp
180 185 190
Ile Ile Gly Val Asp Glu Asn Glu Asp Ser Gln Leu Lys Gly Pro Ala
      195
                         200
                                     205
Asn Ile Phe Asn Lys Phe Ile Glu Glu Asn Phe Pro Asn Leu Lys Lys
            215
                                  220
Glu Met Ser Met Asn Arg Gln Glu Ala Tyr Arg Thr Pro Asn Arg Leu
225 230 235 240
Asp Gln Lys Arg Asn Ser Ser Leu His Ile Ile Ile Arg Thr Thr Asn
             245
                        250
Ala Leu Asn Lys Asp Arg Ile Leu Lys Ala Val Arg Glu Lys Ser Gln
        260
                            265
Val Thr Tyr Lys Gly Arg Pro Ile Arg Ile Thr Pro Asp Phe Ser Pro
       275
                         280
                                            285
Glu Thr Met Lys Ala Arg Arg Ser Trp Thr Asp Val Met Gln Thr Leu
```

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300
   290
                   295
Arg Glu His Lys Cys Gln Pro Arg Leu Leu Tyr Pro Ala Lys Leu Ser 305 310 315 320
                             315
Ile Thr Ile Asp Gly Glu Thr Lys Val Phe His Asp Lys Thr Lys Phe
          325 330
                                     335
Thr Gln Tyr Leu Ser Met Asn Pro Gly Leu Gln Arg Ile Ile Lys Gly 340 345 350
Lys His Gln His Lys Asp Gly Asn Tyr Thr Leu Glu Lys Ala Arg Lys
 355 360 365
Arg Ser Phe Asn Lys Pro Lys Arg Arg Gln Pro Lys
                   375
<210> 679
<211> 210
<212> PRT
<213> Mouse
<400> 679
Tyr Gly Thr His Asn His Cys Trp Leu Ser Leu His Arg Gly Phe Ile
                            10
Trp Ser Phe Leu Gly Pro Ala Ala Ile Ile Leu Ile Asn Leu Val
   20
                         25
Phe Tyr Phe Leu Ile Ile Trp Ile Leu Arg Ser Lys Leu Ser Ser Leu
     35
                      40
                                      45
Asn Lys Glu Val Ser Thr Leu Gln Asp Thr Lys Val Met Thr Phe Lys
          55
                              60
Ala Ile Val Gln Leu Phe Val Leu Gly Cys Ser Trp Gly Ile Gly Leu 65 70 75 80
Phe Ile Phe Ile Glu Val Gly Lys Thr Val Arg Leu Ile Val Ala Tyr
           85
                        90
Leu Phe Thr Ile Ile Asn Val Leu Gln Gly Val Leu Ile Phe Met Val
                         105
   100
                                  110
His Cys Leu Leu Asn Arg Gln Val Arg Met Glu Tyr Lys Lys Trp Phe
  115 120
                               125
His Arg Leu Arg Lys Glu Val Glu Ser Glu Ser Thr Glu Val Ser His
130 135 140
Ser Thr Thr His Thr Lys Met Gly Leu Ser Leu Asn Leu Glu Asn Phe
145 150 155
Cys Pro Thr Gly Asn Leu His Asp Pro Ser Asp Ser Ile Leu Pro Ser
                    170
                                    175
        165
Thr Glu Val Ala Gly Val Tyr Leu Ser Thr Pro Arg Ser His Met Gly
                185
      180
                               190
Ala Glu Asp Val Asn Ser Gly Thr His Ala Tyr Trp Ser Arg Thr Ile
                      200
                                      205
Ser Asp
 210
<210> 680
<211> 373
<212> PRT
<213> Mouse
<400> 680
Met Lys Glu Tyr Val Met Leu Leu Leu Leu Ala Val Cys Ser Ala Lys
          5
                            10 15
Pro Phe Phe Ser Pro Ser His Thr Ala Leu Lys Asn Met Met Leu Lys
         20
                          25.
```

```
40
     35
Leu Phe Pro Thr Lys Glu Pro Val Asn Pro Phe Phe Pro Phe Asp Leu
  50
                55
                                 60
Phe Pro Thr Cys Pro Phe Gly Cys Gln Cys Tyr Ser Arg Val Val His
65
             70
                              75
Cys Ser Asp Leu Gly Leu Thr Ser Val Pro Asn Asn Ile Pro Phe Asp
          85
                          90
Thr Arg Met Val Asp Leu Gln Asn Asn Lys Ile Lys Glu Ile Lys Glu
                 105
       100
                                · 110
Asn Asp Phe Lys Gly Leu Thr Ser Leu Tyr Ala Leu Ile Leu Asn Asn
115 120 125
                              125
Asn Lys Leu Thr Lys Ile His Pro Lys Thr Phe Leu Thr Thr Lys Lys
  130 135
                                  140
Leu Arg Arg Leu Tyr Leu Ser His Asn Gln Leu Ser Glu Ile Pro Leu
145 150
                              155
Asn Leu Pro Lys Ser Leu Ala Glu Leu Arg Ile His Asp Asn Lys Val
          165
                         170
                                           175
Lys Lys Ile Gln Lys Asp Thr Phe Lys Gly Met Asn Ala Leu His Val
    . 180
                      185
                                 190
Leu Glu Met Ser Ala Asn Pro Leu Glu Asn Asn Gly Ile Glu Pro Gly
  . 195
             200 205
Ala Phe Glu Gly Val Thr Val Phe His Ile Arg Ile Ala Glu Ala Lys
  210
                215
                                220
Leu Thr Ser Ile Pro Lys Gly Leu Pro Pro Thr Leu Leu Glu Leu His
       230
                      235
Leu Asp Phe Asn Lys Ile Ser Thr Val Glu Leu Glu Asp Leu Lys Arg
           245
                    250 255
Tyr Arg Glu Leu Gln Arg Leu Gly Leu Gly Asn Asn Arg Ile Thr Asp
        260
                       265
Ile Glu Asn Gly Thr Phe Ala Asn Ile Pro Arg Val Arg Glu Ile His
    275
             280
                              285
Lys Tyr Leu Gln Ile Ile Phe Leu His Tyr Asn Ser Ile Ala Lys Val
305 310 315
Gly Val Asn Asp Phe Cys Pro Thr Val Pro Lys Met Lys Lys Ser Leu
           325
                   330 335
Tyr Ser Ala Ile Ser Leu Phe Asn Asn Pro Met Lys Tyr Trp Glu Ile
       340
                345 350
Gln Pro Ala Thr Phe Arg Cys Val Leu Gly Arg Met Ser Val Gln Leu
   355
                     360
Gly Asn Val Gly Lys
   370
<210> 681
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Met Trp Gly Cys Trp Leu Gly Leu Leu Leu Leu Leu Leu Ala Gly Gln
                           10
Ala Ala Leu Glu Ala Arg Arg Ser Arg Trp Arg Arg Glu Leu Ala Pro
        20
                       25
                                       30
Gly Leu His Leu Arg Gly Ile Arg Asp Ala Gly Gly Arg Tyr Cys Gln
                     40
```

```
Glu Gln Asp Met Cys Cys Arg Gly Arg Ala Asp Glu Cys Ala Leu Pro
                      55
Tyr Leu Gly Ala Thr Cys Tyr Cys Asp Leu Phe Cys Asn Arg Thr Val
                  70
                                   75
Ser Asp Cys Cys Pro Asp Phe Trp Asp Phe Cys Leu Gly Ile Pro Pro
             85
                                90
Pro Phe Pro Val Gln Gly Cys Met His Gly Gly Arg Ile Tyr Pro 100 \hspace{1cm} 105 \hspace{1cm} 105 \hspace{1cm} 110 \hspace{1cm}
Val Phe Gly Thr Tyr Trp Asp Asn Cys Asn Arg Cys Thr Cys His Glu
 115
                     120
                                         125
Gly Gly His Trp Glu Cys Asp Gln Glu Pro Cys Leu Val Asp Pro Asp
            135
                                      140
Met Ile Lys Ala Ile Asn Arg Gly Asn Tyr Gly Trp Gln Ala Gly Asn 145 150 150 155
        150
                                   155
His Ser Ala Phe Trp Gly Met Thr Leu Asp Glu Gly Ile Arg Tyr Arg
             165
                      170
                                                 175
Leu Gly Thr Ile Arg Pro Ser Ser Thr Val Met Asn Met Asn Glu Ile
          180
                           185
                                              190
Tyr Thr Val Leu Gly Gln Gly Glu Val Leu Pro Thr Ala Phe Glu Ala
      195
                       200
                                   205
Ser Glu Lys Trp Pro Asn Leu Ile His Glu Pro Leu Asp Gln Gly Asn 210 215 220
Cys Ala Gly Ser Trp Ala Phe Ser Thr Ala Ala Val Ala Ser Asp Arg
225
        230
                                  235
Val Ser Ile His Ser Leu Gly His Met Thr Pro Ile Leu Ser Pro Gln
        245
                       250
                                          255
Asn Leu Leu Ser Cys Asp Thr His His Gln Gln Gly Cys Arg Gly Gly 260 265 270
Arg Leu Asp Gly Ala Trp Trp Phe Leu Arg Arg Arg Gly Val Val Ser
      275
                        280
Asp Asn Cys Tyr Pro Phe Ser Gly Arg Glu Gln Asn Glu Ala Ser Pro
  290
                   295
                                       300
Thr Pro Arg Cys Met Met His Ser Arg Ala Met Gly Arg Gly Lys Arg
             310
                                 315
Gln Ala Thr Ser Arg Cys Pro Asn Gly Gln Val Asp Ser Asn Asp Ile
 . 325 330
                                         335
Tyr Gln Val Thr Pro Ala Tyr Arg Leu Gly Ser Asp Glu Lys Glu Ile
 . 340
                           345
                                              350
Met Lys Glu Leu Met Glu Asn Gly Pro Val Gln Ala Leu Met Glu Val
 355 360
                                  365
His Glu Asp Phe Phe Leu Tyr Gln Arg Gly Ile Tyr Ser His Thr Pro 370 375 380 ...
Val Ser Gln Gly Arg Pro Glu Gln Tyr Arg Arg His Gly Thr His Ser
                390
                                   395
Val Lys Ile Thr Gly Trp Gly Glu Glu Thr Leu Pro Asp Gly Arg Thr
             405
                                410
                                                   415
Ile Lys Tyr Trp Thr Ala Ala As<br/>n Ser Trp Gly Pro Trp Trp Gly Glu 
          420
                          425
                                              430
Arg Gly His Phe Arg Ile Val Arg Gly Thr Asn Glu Cys Asp Ile Glu
     435
                     440
                                 445
Thr Phe Val Leu Gly Val Trp Gly Arg Val Gly Met Glu Asp Met Gly
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His His
465
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Ala Pro Glu Val Cys Gly Ala Leu Asn Val Thr Val Ser Pro Gly Pro
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Val Val Asp Tyr Leu Glu Gly Glu Asn Ala Thr Leu Leu Cys His Val
      35
                         40
                                            45
Ser Gln Lys Arg Arg Lys Asp Ser Leu Leu Ala Val Arg Trp Phe Phe
                     55
                                        60
Ala Pro Asp Gly Ser Gln Glu Ala Leu Met Val Lys Met Thr Lys Leu
65
               70
                                   75
Arg Ile Ile Gln Tyr Tyr Gly Asn Phe Ser Arg Thr Ala Asn Gln Gln
            85
                           90
Arg Leu Arg Leu Leu Glu Glu Arg Arg Gly Val Leu Tyr Arg Leu Ser
           100
                            105
                                                110
Val Leu Thr Leu Arg Pro Thr Asp Gln Gly Gln Tyr Val Cys Lys Val
                        120
                                           125
Gln Glu Ile Ser Lys His Arg Asn Lys Trp Thr Ala Trp Ser Asn Gly
  130
                     135
                                        140
Ser Ser Ala Thr Glu Met Arg Val Ile Ser Leu Lys Ala Gly Glu Asp
                                 155
                 150
Ser Ser Phe Glu Lys Lys Lys Val Thr Trp Ala Phe Phe Glu Asp Leu
        165
                        170
                                                   175
Tyr Val Tyr Ala Val Leu Val Cys Cys Val Gly Ile Leu Ser Val Leu
         180
                            185
Leu Phe Thr Leu Val Ile Ala Cys Ser Leu Cys Phe Thr Arg Gly Asn
                          200
                                            205
Gln Glu
  210
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Met Asp Phe Trp Leu Trp Leu Leu Tyr Phe Leu Pro Val Ser Gly Ala
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Leu Arg Val Leu Pro Glu Val Gln Leu Asn Val Glu Trp Gly Gly Ser
                            25
                                               30
Ile Ile Ile Glu Cys Pro Leu Pro Gln Leu His Val Arg Met Tyr Leu
      35
                         40
                                           45
Cys Arg Gln Met Ala Lys Pro Gly Ile Cys Ser Thr Val Val Ser Asn
  50
                      55
                                        60
Thr Phe Val Lys Lys Glu Tyr Glu Arg Arg Val Thr Leu Thr Pro Cys
70 75 80
                                 75
Leu Asp Lys Lys Leu Phe Leu Val Glu Met Thr Gln Leu Thr Glu Asn
             85
                              90
                                                   95
Asp Asp Gly Ile Tyr Ala Cys Gly Val Gly Met Lys Thr Asp Lys Gly
          100
                            105
                                          . 110
Lys Thr Gln Lys Ile Thr Leu Asn Val His Asn Glu Tyr Pro Glu Pro
     115
                       120 125
Phe Trp Glu Asp Glu Trp Thr Ser Glu Arg Pro Arg Trp Leu His Arg
   130
                      135
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Phe Leu Gln His Gln Met Pro Trp Leu His Gly Ser Glu His Pro Ser
                  150
                                    155
Ser Ser Gly Val Ile Ala Lys Val Thr Thr Pro Ala Ser Lys Thr Glu
              165
                              170
                                                 175
Ala Pro Pro Val His Gln Pro Ser Ser Ile Thr Ser Val Thr Gln His
          180
                            185
                                       190
Pro Arg Val Tyr Arg Ala Phe Ser Val Ser Ala Thr Lys Ser Pro Ala
  195
               `200 205
Leu Leu Pro Ala Thr Thr Ala Ser Lys Thr Ser Thr Gln Gln Ala Ile
                   215
                                  220
Arg Pro Leu Glu Ala Ser Tyr Ser His His Thr Arg Leu His Glu Gln 225 230 230 235 240
Arg Thr Arg His His Gly Pro His Tyr Gly Arg Glu Asp Arg Gly
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                                 250
                                                   255
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<213> Mouse
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Met Lys Ala Leu Arg Ala Val Leu Leu Ile Leu Leu Leu Ser Gly Gln
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Pro Gly Ser Gly Trp Ala Gln Glu Asp Gly Asp Ala Asp Pro Glu Pro
       20
                          25`
                                               3.0
Glu Asn Tyr Asn Tyr Asp Asp Asp Asp Glu Glu Glu Glu Glu Glu
      35
                         40
                                          45
Thr Asn Met Ile Pro Gly Ser Arg Asp Arg Ala Pro Leu Gln Cys Tyr
                     55
                                      60
Phe Cys Gln Val Leu His Ser Gly Glu Ser Cys Asn Gln Thr Gln Ser
                 70
Cys Ser Ser Ser Lys Pro Phe Cys Ile Thr Leu Val Ser His Ser Gly
              85
                        90
Thr Asp Lys Gly Tyr Leu Thr Thr Tyr Ser Met Trp Cys Thr Asp Thr 100 105 110
Cys Gln Pro Ile Ile Lys Thr Val Gly Gly Thr Gln Met Thr Gln Thr
   115
                    120
                                     125
Cys Cys Gln Ser Thr Leu Cys Asn Ile Pro Pro Trp Gln Asn Pro Gln
  130
                  135
                               140
Val Gln Asn Pro Leu Gly Gly Arg Ala Asp Ser Pro Leu Glu Ser Gly 145 150 150 160
Thr Arg His Pro Gln Gly Gly Lys Phe Ser His Pro Gln Val Lys
            165
                              170
Ala Ala His Pro Gln Ser Asp Gly Ala Asn Leu Pro Lys Ser Gly Lys
          180
                            185
                                              190
Ala Asn Gln Pro Gln Gly Ser Gly Ala Gly Tyr Pro Ser Gly Trp Thr,
                                  205_-
   195
                        200
Lys Phe Gly Asn Ile Ala Leu Leu Leu Ser Phe Phe Thr Cys Leu Trp
  210
                      215
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Ala Ser Gly Ala
225
<210> 685
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<213> Mouse

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Met Ala Ser Gly Trp Phe Tyr Leu Ser Cys Met Val Leu Gly Ser Leu
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Gly Ser Met Cys Ile Leu Phe Thr Ala Tyr Trp Met Gln Tyr Trp Arg
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                           25
                                            30
Gly Gly Phe Ala Trp Asp Gly Thr Val Leu Met Phe Asn Trp His Pro
     35
                       40
Val Leu Met Val Ala Gly Met`Val Val Leu Tyr Gly Ala Ala Ser Leu
 50 55
                               60
Val Tyr Arg Leu Pro Ser Ser Trp Val Gly Pro Arg Leu Pro Trp Lys
65
            70
                                 75
Val Leu His Ala Ala Leu His Leu Leu Ala Phe Thr Cys Thr Val Val
            85 -
                             90 -
Gly Leu Ile Ala Val Phe Arg Phe His Asn His Ser Arg Ile Ala His
          100
                        105
                                            110
Leu Tyr Ser Leu His Ser Trp Leu Gly Ile Thr Thr Val Val Leu Phe
                     120
                                125
Ala Cys Gln Trp Phe Leu Gly Phe Ala Val Phe Leu Leu Pro Trp Ala
  130
                  135 · 140
Ser Gln Trp Leu Arg Ser Leu Leu Lys Pro Leu His Val Phe Phe Gly
145
        150
                         155
Ala Cys Ile Leu Ser Leu Ser Ile Thr Ser Val Ile Ser Gly Ile Asn
           165
                  170
Glu Lys Leu Phe Phe Val Leu Lys Asn Ala Thr Lys Pro Tyr Ser Ser
                          185
        180
Leu Pro Gly Glu Ala Val Phe Ala Asn Ser Thr Gly Leu Leu Val Val
 195
                     200
                                        205
Ala Phe Gly Leu Leu Val Leu Tyr Val Leu Leu Ala Ser Ser Trp Lys
 210
                  215
                                    220
Arg Pro Asp Pro Gly Ala Leu Thr Asp Arg Gln Pro Leu Leu His Asp
225
                230
                                  235
Arg Glu
<210> 686
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<213> Mouse
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Met Arg Leu Pro Leu Pro Leu Leu Leu Phe Gly Cys Arg Ala Ile
       5
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Leu Gly Ser Ala Gly Asp Arg Val Ser Leu Ser Ala Ser Ala Pro Thr
        20
                         25
Leu Asp Asp Glu Glu Lys Tyr Ser Ala His Met Pro Ala His Leu Arg
     35
                       40
                                        ·45
Cys Asp Ala Cys Arg Ala Val Ala Phe Gln Met Gly Gln Arg Leu Ala
  50
                  55
                                     60
Lys Ala Glu Ala Lys Ser His Thr Pro Asp Ala Ser Gly Leu Gln Glu
                 70
                                 75
Leu Ser Glu Ser Thr Tyr Thr Asp Val Leu Asp Gln Thr Cys Ser Gln
            85
                             90
                                              95
Asn Trp Gln Ser Tyr Gly Val His Glu Val Asn Gln Met Lys Arg Leu
         100
                         105
                                          110
Thr Gly Pro Gly Leu Ser Lys Gly Pro Glu Pro Arg Ile Ser Val Met
      115
                      120
                                       125
Ile Ser Gly Gly Pro Trp Pro Asn Arg Leu Ser Lys Thr Cys Phe His
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130
                     135
                                       140
Tyr Leu Gly Glu Phe Gly Glu Asp Gln Ile Tyr Glu Ala Tyr Arg Gln
              150 . 155
Gly Gln Ala Asn Leu Glu Ala Leu Leu Cys Gly Gly Thr His Gly Pro
                          170
             165
Cys Ser Gln Glu Ile Leu Ala Gln Arg Glu Glu Leu
          180
               185
<210> 687
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Met Ile Pro Gln Val Val Thr Ser Glu Thr Val Thr Val Ile Ser Pro
1.
              5
                               10
Asn Gly Ile Ser Phe Pro Gln Thr Asp Lys Pro Gln Pro Ser His Gln
         20
                           25
                                             30
Ser Gln Asp Arg Leu Lys Lys His Leu Lys Ala Glu Ile Lys Val Met
    35
                     40
                                         45
Ala Ala Ile Gln Ile Met Cys Ala Val Met Val Leu Ser Leu Gly Ile
                  55
                                     60 -
Ile Leu Ala Ser Val Pro Ser Asn Leu His Phe Thr Ser Val Phe Ser
              70
                              75
Ile Leu Leu Glu Ser Gly Tyr Pro Phe Val Gly Ala Leu Phe Phe Ala
             85
                              - 90
Ile Ser Gly Ile Leu Ser Ile Val Thr Glu Lys Lys Met Thr Lys Pro
         100
                          105
                                             110
Leu Val His Ser Ser Leu Ala Leu Ser Ile Leu Ser Val Leu Ser Ala
      115
                       120
Leu Thr Gly Ile Ala Ile Leu Ser Val Ser Leu Ala Ala Leu Glu Pro
                    135
  130
                                      140
Ala Leu Gln Gln Cys Lys Leu Ala Phe Thr Gln Leu Asp Thr Thr Gln
                150
145
                                 155
                                                     160
Asp Ala Tyr His Phe Phe Ser Pro Glu Pro Leu Asn Ser Cys Phe Val
            165
                              170
                                                 175
Ala Lys Ala Ala Leu Thr Gly Val Phe Ser Leu Met Leu Ile Ser Ser
180
                         185
                                    190
Val Leu Glu Leu Gly Leu Ala Val Leu Thr Ala Thr Leu Trp Trp Lys
                       200
  195
                                         205
Gln Ser Ser Ser Ala Phe Ser Gly Asn Val Ile Phe Leu Ser Gln Asn
            215
                                     220
Ser Lys Asn Lys Ser Ser Val Ser Ser Glu Ser Leu Cys Asn Pro Thr
225 230
                                   235
Tyr Glu Asn Ile Leu Thr Ser
              245
<210> 688
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Tyr Gln Arg Arg Ser Lys Thr Leu Glu Glu Leu Ala Asn Asp Ile Lys
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Glu Asp Ala Ile Ala Pro Arg Thr Leu Pro Trp Thr Lys Gly Ser Asp
       , 20
                            25.
                                              30
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Thr Ile Ser Lys Asn Gly Thr Leu Ser Ser Val Thr Ser Ala Arg Ala
                        40
                                      45
Leu Arg Pro Pro Lys Ala Ala Pro Pro Arg Pro Gly Thr Phe Thr Pro
  50
                   55
                                    60
Thr Pro Ser Val Ser Ser Gln Ala Leu Ser Ser Pro Arg Leu Pro Arg
               70
                                75
Val Asp Glu Pro Pro Pro Gln Ala Val Ser Leu Thr Pro Gly Gly Val
85 90 95
Ser Ser Ser Ala Leu Ser Arg Met Gly Ala Val Pro Val Met Val Pro
      100
                105
Ala Gln Ser Gln Ala Gly Ser Leu Val
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                      120
<210> 689
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<213> Mouse
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Pro Ala Phe Ser Ser Ala Ala Met Ser Trp Ser Pro Ile Leu Pro Phe 1 5 10 . 15
Leu Ser Leu Leu Leu Leu Phe Pro Leu Glu Val Pro Arg Ala Ala
 20
                        25
                                          30
Thr Ala Ser Leu Ser Gln Ala Ser Ser Glu Gly Thr Thr Thr Cys Lys
                     40
  35
                                        45
Val His Asp Val Cys Leu Leu Gly Pro Arg Pro Leu Pro Pro Ser Pro
 50 55
                            60
Pro Val Arg Val Ser Leu Tyr Tyr Glu Ser Leu Cys Gly Ala Cys Arg
       70
65
                          75
Tyr Phe Leu Val Arg Asp Leu Phe Pro Thr Trp Leu Met Val Met Glu
          85
                     90
Ile Met Asn Ile Thr Leu Val Pro Tyr Gly Asn Ala Gln Glu Arg Asn
         100
                         105
                                           110
Val Ser Gly Thr Trp Glu Phe Thr Cys Gln His Gly Glu Leu Glu Cys
115 120 125
Arg Leu Asn Met Val Glu Ala Cys Leu Leu Asp Lys Leu Glu Lys Glu
  130 135 . 140
Ala Ala Phe Leu Thr Ile Val Cys Met Glu Glu Met Asp Asp Met Glu
                              155
145 150
Lys Lys Leu Gly Pro Cys Leu Gln Val Tyr Ala Pro Glu Val Ser Pro
        165
                     170
                                              175
Glu Ser Ile Met Glu Cys Ala Thr Gly Lys Arg Gly Thr Gln Leu Met
180 185 190
His Glu Asn Ala Gln Leu Thr Asp Ala Leu His Pro Pro His Glu Tyr
    195 200 205
Val Pro Trp Val Leu Val Asn Glu Lys Pro Leu Lys Asp Pro Ser Glu
  210 .
                 215
                                  220
Leu Leu Ser Ile Val Cys Gln Leu Asp Gln Gly Thr Glu Lys Pro Asp
225 230
                               235 240
Ile Cys Ser Ser Ile Ala Asp Ser Pro Arg Lys Val Cys Tyr Lys
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                              250
                                               255
<210> 690
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Met Val Trp Thr Gln Asp Arg Leu His Asp Arg Gln Arg Val Val His
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Trp Asp Leu Ser Gly Asp Pro Gly Ser Gln Arg Arg Arg Leu Val Asp
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Met Tyr Ser Ala Gly Glu Gln Arg Val Tyr Glu Pro Arg Asp Arg Asp 40 45
Arg Leu Leu Ser Pro Ser Ala Phe His Asp Gly Asn Phe Ser Leu
 50
                   55
                                    60
Leu Ile Arg Ala Val Glu Arg Gly Asp Glu Gly Val Tyr Thr Cys Asn
              70
                                   75
Leu His His His Tyr Cys His Leu Asp Glu Ser Leu Ala Val Arg Leu
85 90 95
                               90
Glu Val Thr Asp Asp Pro Leu Leu Ser Arg Ala Tyr Trp Asp Gly Glu
100 105 110
Lys Glu Val Leu Val Val Ala His Gly Ala Pro Ala Leu Met Thr Cys
  115
                       120
                                         125
Ile Asn Arg Ala His Val Trp Thr Asp Arg His Leu Glu Glu Ala Gln
          . 135
                              140
Gln Val Val His Trp Asp Arg Gln Leu Pro Gly Val Ser His Asp Arg 145 150 150 155 160
Ala Asp Arg Leu Leu Asp Leu Tyr Ala Ser Gly Glu Arg Arg Ala Tyr
            165 170
Gly Pro Pro Phe Leu Arg Asp Arg Val Ser Val Asn Thr Asn Ala Phe
         180
                         185
                                     190
Ala Arg Gly Asp Phe Ser Leu Arg Ile Asp Glu Leu Glu Arg Ala Asp
     195
               200
                                 205
Glu Gly Ile Tyr Ser Cys His Leu His His His Tyr Cys Gly Leu His
   210
                   215
                               220
Glu Arg Arg Val Phe His Leu Gln Val Thr Glu Pro Ala Phe Glu Pro
225
       230
                                 235
Pro Ala Arg Ala Ser Pro Gly Asn Gly Ser Gly His Ser Ser Ala
           245
                                250
<210> 691
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<212> PRT
<213> Mouse
<400> 691
Met Lys Leu Lys Gln Arg Val Val Leu Leu Ala Ile Leu Leu Val Ile
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Phe Ile Phe Thr Lys Val Phe Leu Ile Asp Asn Leu Asp Thr Ser Ala
       20
                           25
Ala Asn Arg Glu Asp Gln Arg Ala Phe His Arg Met Met Thr Gly Leu
   35
                        40
                                         45
Arg Val Glu Leu Val Pro Lys Leu Asp His Thr Leu Gln Ser Pro Trp
                  55
                                    60
Glu Ile Ala Ala Gln Trp Val Val Pro Arg Glu Val Tyr Pro Glu Glu
                 70
                                  75
Thr Pro Glu Leu Gly Ala Ile Met His Ala Met Ala Thr Lys Lys Ile
            85
                             90
Ile Lys Ala Asp Val Gly Tyr Lys Gly Thr Gln Leu Lys Ala Leu Leu
         100
                          105
                                            110
Ile Leu Glu Gly Gly Gln Lys Val Val Phe Lys Pro Lys Arg Tyr Ser
      115
                       120
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Arg Asp Tyr Val Val Glu Gly Glu Pro Tyr Ala Gly Tyr Asp Arg His

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130
                      135
                                         140
Asn Ala Glu Val Ala Ala Phe His Leu Asp Arg Ile Leu Gly Phe Arg
145 . 150 155
Arg Ala Pro Leu Val Val Gly Arg Tyr Val Asn Leu Arg Thr Glu Val
        165
                          170
                                          175
Lys Pro Val Ala Thr Glu Gln Leu Leu Ser Thr Phe Leu Thr Val Gly 180 185 190
Asn Asn Thr Cys Phe Tyr Gly Lys Cys Tyr Tyr Cys Arg Glu Thr Glu
195 200 205
Pro Ala Cys Ala Asp Gly Asp Met Met Glu Gly Ser Val Thr Leu Trp
  210
                     215
                                    220
Leu Pro Asp Val Trp Pro Leu Gln Lys His Arg His Pro Trp Gly Arg
                 230
                            235
Thr Tyr Arg Glu Gly Lys Leu Ala Arg Trp Glu Tyr Asp Glu Ser
              245
                                 250
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<400> 692
Met Gln Thr Met Trp Gly Ser Gly Glu Leu Leu Val Ala Trp Phe Leu
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Val Leu Ala Ala Asp Gly Thr Thr Glu His Val Tyr Arg Pro Ser Arg
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                             25
Arg Val Cys Thr Val Gly Ile Ser Gly Gly Ser Ile Ser Glu Thr Phe 35 40 45
Val Gln Arg Val Tyr Gln Pro Tyr Leu Thr Thr Cys Asp Gly His Arg 50 55 60
 50 55
Ala Cys Ser Thr Tyr Arg Thr Ile Tyr Arg Thr Ala Tyr Arg Arg Ser
                70
                                  75
Pro Gly Val Thr Pro Ala Arg Pro Arg Tyr Ala Cys Cys Pro Gly Trp
            85
                               90
                                                  95
Lys Arg Thr Ser Gly Leu Pro Gly Ala Cys Gly Ala Ala Ile Cys Gln 100 105 110
Pro Pro Cys Gly Asn Gly Gly Ser Cys Ile Arg Pro Gly His Cys Arg 115 120 125
Cys Pro Val Gly Trp Gln Gly Asp Thr Cys Gln Thr Asp Val Asp Glu
 130
                    135
                                    140
Cys Ser Thr Gly Glu Ala Ser Cys Pro Gln Arg Cys Val Asn Thr Val 145 150 155 __160
Gly Ser Tyr Trp Cys Gln Gly Trp Glu Gly Gln Ser Pro Ser Ala Asp
165 170 175
Gly Thr Arg Cys Leu Ser Lys Glu Gly Pro Ser Pro Val Ala Pro Asn
         180
                         185
                                    190
Pro Thr Ala Gly Val Asp Ser Met Ala Arg Glu Glu Val Tyr Arg Leu
     195 . 200
                                   205
Gln Ala Arg Val Asp Val Leu Glu Gln Lys Leu Gln Leu Val Leu Ala
210 215 220
Pro Leu His Ser Leu Ala Ser Arg Ser Thr Glu His Gly Leu Gln Asp
             230
                           235
Pro Gly Ser Leu Leu Ala His Ser Phe Gln Gln Leu Asp Arg Ile
              245
                                 250
<210> 693
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<212> PRT <213> Mouse <400> 693 Met Arg Leu Thr Val Gly Ala Leu Leu Ala Cys Ala Ala Leu Gly Leu 10 Cys Leu Ala Val Pro Asp Lys Thr Val Lys Trp Cys Ala Val Ser Glu 20 25 30 His Glu Asn Thr Lys Cys Ile Ser Phe Arg Asp His Met Lys Thr Val 45 35 40 Leu Pro Pro Asp Gly Pro Arg Leu Ala Cys Val Lys Lys Thr Ser Tyr 55 Pro Asp Cys Ile Lys Ala Ile Ser Ala Ser Glu Ala Asp Ala Met Thr 70 75 Leu Asp Gly Gly Trp Val Tyr Asp Ala Gly Leu Thr Pro Asn Asn Leu 90 85 Lys Pro Val Ala Ala Glu Phe Tyr Gly Ser Val Glu His Pro Gln Thr 100 105 110 Tyr Tyr Tyr Ala Val Ala Val Val Lys Lys Gly Thr Asp Phe Gln Leu 115 120 125 Asn Gln Leu Glu Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser 130 135 140 Ala Gly Trp Val Ile Pro Ile Gly Leu Leu Phe Cys Lys Leu Ser Glu 150 155 Pro Arg Ser Pro Leu Glu Lys Ala Val Ser Ser Phe Phe Ser Gly Ser 175 165 170 Cys Val Pro Cys Ala Asp Pro Val Ala Phe Pro Lys Leu Cys Gln Leu 180 185 190 Cys Pro Gly Cys Gly Cys Ser Ser Thr Gln Pro Phe Phe Gly Tyr Val . 200 205 195 Gly Ala Phe Lys Cys Leu Lys Asp Gly Gly Gly Asp Val Ala Phe Val 210 215 220 Lys His Thr Thr Ile Phe Glu Val Leu Pro Glu Lys Ala Asp Arg Asp 230 235 Gln Tyr Glu Leu Leu Cys Leu Asp Asn Thr Arg Lys Pro Val Asp 250 255 <210> 694 <211> 255 <212> PRT <213> Mouse <400> 694 Gly Ala Pro Thr Pro Ala Tyr Val Arg Ser Ala Arg Arg Thr Glu Pro 10 · 15 Leu Ala Ser Gly Ala Arg Ser Arg Leu Cys Gln Cys Arg Arg Val Pro 20 25 -·30 Ala Arg Lys Gln Gly Pro Gln Glu Gln Gly Gly Ser Gly Glu Ser Thr 45 35 40 Thr Ser Ser Pro Gln Trp Trp Arg Arg Trp Arg Arg Leu Trp Ser Thr 50 55 60 Cys Ser Cys Ser Ala Asp Asp Arg His Thr Gly Ser His Thr Asp Leu 70 75 Lys Glu Glu Thr Pro Ser Trp Thr Gln Ile Ser Val Val Phe Arg Lys 85 90 95 Asp Gly Gln Asp Glu Leu Gln Ala Ala His Lys Ala His Gly Ser Gly

110

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Ser Pro Leu Thr Asn Gln Glu Ile Pro Ser Ser Ser Gly Ser Gly Phe
     115
                       120
                                 125
Ile Val Ser Glu Asp Gly Leu Ile Val Thr Asn Ala His Val Leu Thr
  130
                    135
                                   140
Asn Gln Gln Lys Ile Gln Val Glu Leu Gln Ser Gly Ala Arg Tyr Glu
               150
                             155
Ala Thr Val Lys Asp Ile Asp His Lys Leu Asp Leu Ala Leu Ile Lys
165 170 175
             165
                              170
                                       175
Ile Glu Pro Asp Thr Glu Leu Pro Val Leu Leu Gly Arg Ser Ser
         180
                          185
                                    190
Asp Leu Arg Ala Gly Glu Phe Val Val Ala Leu Gly Ser Pro Phe Ser
  195
                     200
                                          205
Leu Gln Asn Thr Val Thr Ala Gly Ile Val Ser Thr Thr Gln Arg Gly 210 215 220
Gly Arg Glu Leu Gly Leu Lys Asn Ser Asp Ile Asp Tyr Ile Gln Thr
225 230 235
Asp Ala Ile Ile Asn His Gly Asn Ser Gly Gly Pro Leu Val Asn
              245
                                250
<210> 695
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<400> 695
Met Pro Ala Cys Arg Leu Cys Leu Leu Ala Ala Gly Leu Leu Gly
             5
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Leu Leu Leu Phe Thr Pro Ile Ser Ala Thr Gly Thr Asp Ala Glu Lys
  20
                            25
                                             30
Pro Gly Glu Cys Pro Gln Leu Glu Pro Ile Thr Asp Cys Val Leu Glu
                      40
                                         45
Cys Thr Leu Asp Lys Asp Cys Ala Asp Asn Arg Lys Cys Cys Gln Ala
  50
                    55
                                      60
Gly Cys Ser Ser Val Cys Ser Lys Pro Asn Gly Pro Ser Glu Gly Glu
                70
                                75
Leu Ser Gly Thr Asp Thr Lys Leu Ser Glu Thr Gly Thr Thr Thr Gln
             85
                              90
Ser Ala Gly Leu Asp His Thr Thr Lys Pro Pro Gly Gly Gln Val Ser
         100
                           105
                                            110
Thr Lys Pro Pro Ala Val Thr Arg Glu Gly Leu Gly Val Arg Glu Lys
    115
                      120
                                         125
Gln Gly Thr Cys Pro Ser Val Asp Ile Pro Lys Leu Gly Leu Cys Glu
  130
                   135
                                     140
Asp Gln Cys Gln Val Asp Ser Gln Cys Ser Gly Asn Met Lys Cys Cys
        150
                          155
Arg Asn Gly Cys Gly Lys Met Ala Cys Thr Thr Pro Lys Phe
            165
                               170
<210> 696
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<212> PRT
<213> Mouse
<400> 696
Leu Ala Thr Leu Val Gln Val Ser Arg Ile Arg Ala Tyr Ser Gln Gly
            5
                       10
Gln Thr Gln Asp Gln Gln Gly Ser Ser Ser Leu Asp Lys Val Ala Val
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20
Pro Arg Glu Gln Thr His Ser Gly Leu Glu Gln Ile Gln Gln Ile Gln
  35
                         40
Gln Gln Leu Thr Gln Phe Asn Ala Ser Leu Ala Gly Leu Cys Arg Pro
  50
                     55
Cys Pro Trp Asp Trp Glu Leu Phe Gln Gly Ser Cys Tyr Leu Phe Ser 65 75 80
Arg Thr Leu Gly Ser Trp Glu Thr Ser Ala Ser Ser Cys Glu Asp Leu
             85
                             90
Gly Ala His Leu Val Ile Val Asn Ser Val Ser Glu Gln Arg Phe Met
        100
                   105
                                               110
Lys Tyr Trp Asn Val Arg Lys Asn Gln Arg Ser Trp Ile Gly Leu Ser
115 120 125
Asp His Ile His Glu Gly Ser Trp Gln Trp Val Asp Gly Ser Ala Leu
  130 135
                              140
Lys Phe Ser Phe Trp Lys Glu Gly Glu Pro Asn Asn Asp Gly Asp Glu
                150
                                155
Asp Cys Val Glu Leu Phe Met Asp Asp Trp Asn Asp Asn Lys Cys Thr
             165
                                170
                                                  175
Glu Gln Asn Phe Trp Val Cys Glu Gln Pro Ser Ala Pro Cys Pro His
                              185
<210> 697
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Val Arg Asn Gly Asp Leu Phe Phe Lys Lys Val Gln Val Glu Asp Gly
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Gly Val Tyr Thr Cys Tyr Ala Met Gly Glu Thr Phe Asn Glu Thr Leu
        20.
                            25
Ser Val Glu Leu Lys Val Tyr Asn Phe Thr Leu His Gly His His Asp
    35
                         40
                                           45
Thr Leu Asn Thr Ala Tyr Thr Thr Leu Val Gly Cys Ile Leu Ser Val
 . 50
                  55
                                       60
Val Leu Val Leu Ile Tyr Leu Tyr Leu Thr Pro Cys Arg Cys Trp Cys 65 70 75 80
Arg Gly Val Glu Lys Pro Ser Ser His Gln Gly Asp Ser Leu Ser Ser 85 90 95
Ser Met Leu Ser Thr Thr Pro Asn His Asp Pro Met Ala Gly Gly Asp
                                      · 110
         100
                   105
Lys Asp Asp Gly Phe Asp Arg Arg Val Ala Phe Leu Glu Pro Ala Gly
      115
                         120
                                          125
Pro Gly Gln Gly Gln Asn Gly Lys Leu Lys Pro Gly Asn Thr Leu Pro
  130
                   135
                               140
Val Pro Glu Ala Thr Gly Lys Gly Gln Arg Arg Met Ser Asp Pro Glu
                 150
                                   155
Ser Val Ser Ser Val-Phe Ser Asp Thr Pro Ile Val Val
              165
                                 170
<210> 698
<211> 88
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<212> PRT <213> Mouse

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Met Glu Glu Ile Thr Cys Ala Phe Leu Leu Leu Ala Gly Leu Pro
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Ala Leu Glu Ala Ser Asp Pro Val Asp Lys Asp Ser Pro Phe Tyr Tyr
           20
                             25
                                                 30
Asp Trp Glu Ser Leu Gln Leu Gly Gly Leu Ile Phe Gly Gly Leu Leu
                         `40
                                            45
Cys Ile Ala Gly Ile Ala Met Ala Leu Ser Gly Lys Cys Lys Cys Arg
                      55
                                         60
Arg Thr His Lys Pro Ser Ser Leu Pro Gly Lys Ala Thr Pro Leu Ile
Ile Pro Gly Ser Ala Asn Thr Cys
               85
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<400> 699
Met Tyr Ser Glu Gly Ala Pro Phe Trp Thr Gly Ile Val Ala Met Leu
               5
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Ala Gly Ala Val Ala Phe Leu His Lys Lys Arg Gly Gly Thr Cys Trp
           20
                              25
                                                  30
Ala Leu Met Arg Thr Leu Leu Val Leu Ala Ser Phe Cys Thr Ala Val
      35
                          40
Ala Ala Ile Val Ile Gly Ser Arg Glu Leu Asn Tyr Tyr Trp Tyr Phe
  50
                    • 55
                                         60
Leu Gly Asp Asp Val Cys Gln Arg Asp Ser Ser Tyr Gly Trp Ser Thr
                 70
65
                                     75
Met Pro Arg Thr Thr Pro Val Pro Glu Glu Ala Asp Arg Ile Ala Leu
            85
                                90
Cys Ile Tyr Tyr Thr Ser Met Leu Lys Thr Leu Leu Met Ser Leu Gln
           100
                             105
                                                110
Ala Met Leu Gly Ile Trp Val Leu Leu Leu Ala Ser Leu Thr
                        120
                                        125
Pro Val Cys Val Tyr Ile Trp Lys Arg Phe Phe Thr Lys Ala Glu Thr
  130
                      135
Glu Glu Lys Lys Leu Leu Gly Ala Ala Val Ile
                   150
145
<210> 700
<211> 255
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<213> Mouse
<400> 700
Met Leu Gln His Thr Ser Leu Val Leu Leu Leu Ala Ser Ile Trp Thr
               5 .
1
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Thr Arg His Pro Val Gln Gly Ala Asp Leu Val Gln Asp Leu Ser Ile
          20
                              25
Ser Thr Cys Arg Ile Met Gly Val Ala Leu Val Gly Arg Asn Lys Asn
                         40
Pro Gln Met Asn Phe Thr Glu Ala Asn Glu Ala Cys Lys Met Leu Gly
                       55
                                         60
Leu Thr Leu Ala Ser Arg Asp Gln Val Glu Ser Ala Gln Lys Ser Gly
```

```
65
                  70
                                                       80
Phe Glu Thr Cys Ser Tyr Gly Trp Val Gly Glu Gln Phe Ser Val Ile
              85
                               90
Pro Arg Ile Phe Ser Asn Pro Arg Cys Gly Lys Asn Gly Lys Gly Val
        100
                   105
                                               110
Leu Ile Trp Asn Ala Pro Ser Ser Gln Lys Phe Lys Ala Tyr Cys His
Asn Ser Ser Asp Thr Trp Val Asn Ser Cys Ile Pro Glu Ile Val Thr
  130 135
                                    140
Thr Phe Tyr Pro Val Leu Asp Thr Gln Thr Pro Ala Thr Glu Phe Ser
145
                150
                                   155
Val Ser Ser Ser Ala Tyr Leu Ala Ser Ser Pro Asp Ser Thr Thr Pro
             165
                          170
                                                  175
Val Ser Ala Thr Thr Arg Ala Pro Pro Leu Thr Ser Met Ala Arg Lys
         180
                            185
                                      190
Thr Lys Lys Ile Cys Ile Thr Glu Val Tyr Thr Glu Pro Ile Thr Met
     195
                        200
                                         205
Ala Thr Glu Thr Glu Ala Phe Val Ala Ser Gly Ala Ala Phe Lys Asn
  210
                     215
                                       220
Glu Ala Ala Gly Phe Gly Gly Val Pro Thr Ala Leu Leu Val Leu Ala
225
                230
                            235
Leu Leu Phe Phe Gly Ala Ala Ala Val Leu Ala Val Cys Tyr Val
              245
                                250
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Met Val Trp Ala Asn Leu Ala Val Phe Val Ile Cys Phe Leu Pro Leu
              5
                                10
His Val Val Leu Thr Val Gln Val Ser Leu Asn Leu Asn Thr Cys Ala
        20
                            25
                                               30
Ala Arg Asp Thr Phe Ser Arg Ala Leu Ser Ile Thr Gly Lys Leu Ser
      35
                        40
                                          45
Asp Thr Asn Cys Cys Leu Asp Ala Ile Cys Tyr Tyr Tyr Met Ala Arg
 - 50
                    55
                                      60
Glu Phe Gln Glu Ala Ser Lys Pro Ala Thr Ser Ser Asn Thr Pro His
                 70
Lys Ser Gln Asp Ser Gln Ile Leu Ser Leu Thr
              85
<210> 702
<211> 244
<212> PRT
<213> Mouse
<400> 702
Gly Trp Gln Gly Ala Pro Asp Pro Arg Gly Leu Gly Gln Leu Ser Gln
              5
                               10
Pro Tyr Met Gly Gly Glu Met Pro Trp Thr Ile Leu Leu Phe Ala Ser
          20
                            25
                                       . 30
Gly Ser Leu Ala Ile Pro Ala Pro Ser Ile Ser Leu Val Pro Pro Tyr
                      40
                                45
Pro Ser Ser His Glu Asp Pro Ile Tyr Ile Ser Cys Thr Ala Pro Gly
   50
```

```
Asp Ile Leu Gly Ala Asn Phe Thr Leu Phe Arg Gly Gly Glu Val Val
                 70 -
                                 75
Gln Leu Leu Gln Ala Pro Ser Asp Arg Pro Asp Val Thr Phe Asn Val
             85
                             90
Thr Gly Gly Gly Gly Gly Gly Glu Ala Ala Gly Gly Asn Phe
         100
                       105
Cys Cys Gln Tyr Gly Val Met Gly Glu His Ser Gln Pro Gln Leu Ser
115 120 125
Asp Phe Ser Gln Gln Val Gln Val Ser Phe Pro Val Pro Thr Trp Ile
 130 135
                            140
Leu Ala Leu Ser Leu Ser Leu Ala Gly Ala Val Leu Phe Ser Gly Leu
145 . 150
                       155
Val Ala Ile Thr Val Leu Val Arg Lys Ala Lys Ala Lys Asn Leu Gln
165 170 175
Lys Gln Arg Glu Arg Glu Ser Cys Trp Ala Gln Ile Asn Phe Thr Asn
        180
                         185
Thr Asp Met Ser Phe Asp Asn Ser Leu Phe Ala Ile Ser Thr Lys Met
      195
                     200
                                       205
Thr Gln Glu Asp Ser Val Ala Thr Leu Asp Ser Gly Pro Arg Lys Arg
 210 215
                             220
Pro Thr Ser Ala Ser Ser Ser Pro Glu Pro Pro Glu Phe Ser Thr Phe
225 · 230
                                  235
Arg Ala Cys Gln
<210> 703
<211> 255
<212> PRT
<213> Mouse
<400> 703
Met Ala Gln Leu Ala Arg Ala Thr Arg Ser Pro Leu Ser Trp Leu Leu
            5
                              10
Leu Leu Phe Cys Tyr Ala Leu Arg Lys Ala Gly Gly Asp Ile Arg Val
       20
                          25
Leu Val Pro Tyr Asn Ser Thr Gly Val Leu Gly Gly Ser Thr Thr Leu
    35 40
                                        45
His Cys Ser Leu Thr Ser Asn Glu Asn Val Thr Ile Thr Gln Ile Thr
                 55
                                   60
Trp Met Lys Lys Asp Ser Gly Gly Ser His Ala Leu Val Ala Val Phe
               70
                                75
His Pro Lys Lys Gly Pro Asn Ile Lys Glu Pro Glu Arg Val Lys Phe
            85
                             90
Leu Ala Ala Gln Gln Asp Leu Arg Asn Ala Ser Leu Ala Ile Ser Asn 100 '105 110
Leu Ser Val Glu Asp Glu Gly Ile Tyr Glu Cys Gln Ile Ala Thr Phe
 115 120
                              125.
Pro Arg Gly Ser Arg Ser Thr Asn Ala Trp Leu Lys Val Gln Ala Arg
130 135 140
Pro Lys Asn Thr Ala Glu Ala Leu Glu Pro Ser Pro Thr Leu Ile Leu
145 150 155
Gin Asp Val Ala Lys Cys Ile Ser Ala Asn Gly His Pro Pro Gly Arg
            165
                                   · 175
                            170
Ile Ser Trp Pro Ser Asn Val Asn Gly Ser His Arg Glu Met Lys Glu
```

180

195

205

185 190

Pro Gly Ser Gln Pro Gly Thr Thr Thr Val Thr Ser Tyr Leu Ser Met

```
Val Pro Ser Arg Gln Ala Asp Gly Lys Asn Ile Thr Cys Thr Val Glu
  210
                   215
                                     220
His Glu Ser Leu Gln Glu Leu Asp Gln Leu Leu Val Thr Leu Ser Gln
225
                230
                                235
Pro Tyr Pro Pro Glu Asn Val Ser Ile Ser Gly Tyr Asp Gly Asn
              245
                               250
                                                 255
<210> 704
<211> 255
<212> PRT
<213> Mouse
<400> 704
Met Phe Leu Val Gly Ser Leu Val Val Leu Cys Gly Leu Leu Ala His
 1
              5
                               10
Ser Thr Ala Gln Leu Ala Gly Leu Pro Leu Pro Leu Gly Gln Gly Pro
  20
                          25
Pro Leu Pro Leu Asn Gln Gly Pro Pro Leu Pro Leu Asn Gln Gly Gln
 35
                        40
Leu Leu Pro Leu Ala Gln Gly Leu Pro Leu Ala Val Ser Pro Ala Leu
 50
       55
                               60
Pro Ser Asn Pro Thr Asp Leu Leu Ala Gly Lys Phe Thr Asp Ala Leu
65 70
                        75
Ser Gly Gly Leu Leu Ser Gly Gly Leu Leu Gly Ile Leu Glu Asn Ile
            85
                              90
                                               95
Pro Leu Leu Asp Val Ile Lys Ser Gly Gly Gly Asn Ser Asn Gly Leu
         100
                         105 110
Val Gly Gly Leu Leu Gly Lys Leu Thr Ser Ser Val Pro Leu Leu Asn
      115
                        120
                                 125
Asn Ile Leu Asp Ile Lys Ile Thr Asp Pro Gln Leu Leu Glu Leu Gly
  130
                    135
                                   140
Leu Val Gln Ser Pro Asp Gly His Arg Leu Tyr Val Thr Ile Pro Leu
145
             150
                                 155
                                                  160
Gly Leu Thr Leu Asn Val Asn Met Pro Val Val Gly Ser Leu Leu Gln 165 170 175
Leu Ala Val Lys Leu Asn Ile Thr Ala Glu Val Leu Ala Val Lys Asp
        180 185
                                190
Asn Gln Gly Arg Ile His Leu Val Leu Gly Asp Cys Thr His Ser Pro
      195
                     200
                                        205
Gly Ser Leu Lys Ile Ser Leu Leu Asn Gly Val Thr Pro Val Gln Ser
  210
                   215 .220
Phe Leu Asp Asn Leu Thr Gly Ile Leu Thr Lys Val Leu Pro Glu Leu
225 230
                                235
Ile Gln Gly Lys Val Cys Pro Leu Val Asn Gly Ile Leu Ser Gly
             245
                              250
                                               255
<210> 705
<211> 255
<212> PRT
<213> Mouse
<400> 705
Met Ala Thr Thr Cys Gln Val Val Gly Leu Leu Leu Ser Leu Leu
              5
                              10
Gly Leu Ala Gly Cys Ile Ala Ala Thr Gly Met Asp Met Trp Ser Thr
                                          . 30
          20
                           25
Gln Asp Leu Tyr Asp Asn Pro Val Thr Ala Val Phe Gln His Glu Gly
```

45

```
Leu Trp Arg Ser Cys Val Gln Gln Ser Ser Gly Phe Thr Glu Cys Arg
  50
                    55
Pro Tyr Phe Thr Ile Leu Gly Leu Pro Ala Met Leu Gln Ala Val Arg
                 70
                                     75
Ala Leu Met Ile Val Gly Ile Val Leu Gly Val Ile Gly Ile Leu Val
85 90 95
Ser Ile Phe Ala Leu Lys Cys'Ile Arg Ile Gly Ser Met Asp Asp Ser
                           105
                                       110
Ala Lys Ala Lys Met Thr Leu Thr Ser Gly Ile Leu Phe Ile Ile Ser
                         120.
       115
                                      125
Gly Ile Cys Ala Ile Ile Gly Val Ser Val Phe Ala Asn Met Leu Val
   130
                   135
                               140
Thr Asn Phe Trp Met Ser Thr Ala Asn Met Tyr Ser Gly Met Gly Gly
145 150
                            155
                                                      160
Met Gly Gly Met Val Gln Thr Val Gln Thr Arg Tyr Thr Phe Gly Ala
          165
                               170
                                                 175
Ala Leu Phe Val Gly Trp Val Ala Gly Gly Leu Thr Leu Ile Gly Gly
        180
                            185
                                              190
Val Met Met Cys Ile Ala Cys Arg Gly Leu Thr Pro Asp Asp Ser Asn
195 200 205
Phe Lys Ala Val Ser Tyr His Ala Ser Gly Gln Asn Val Ala Tyr Arg
  210 215
                               220
Pro Gly Gly Phe Lys Ala Ser Thr Gly Phe Gly Ser Asn Thr Arg Asn
                230
                                  235
Lys Lys Ile Tyr Asp Gly Gly Ala Arg Thr Glu Asp Asp Glu Gln
                                 250
<210> 706
<211> 255
<212> PRT
<213> Mouse
<400> 706
Met Gly Arg Phe Ala Ala Ala Leu Val Gly Ser Leu Phe Trp Leu Gly
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                                10
                                          . 15
Leu Leu Cys Gly Leu Gly Ser Leu Ala Ser Ala Glu Pro Arg Ala
 . 20
                            25
Pro Pro Asn Arg Ile Ala Ile Val Gly Ala Gly Ile Gly Gly Thr Ser
 35
                         40
Ser Ala Tyr Tyr Leu Arg Lys Lys Phe Gly Lys Asp Val Lys Ile Asp
50 55
                    55
Val Phe Glu Arg Glu Glu Val Gly Gly Arg Leu Ala Thr Leu Lys Val
65 70 75 80
Gln Gly His Asp Tyr Glu Ala Gly Gly Ser Val Ile His Pro Leu Asn
              85
                                90
                                               95
Leu His Met Lys Arg Phe Val Lys Glu Leu Gly Leu Ser Ser Val Pro
         100
                            105
                                        110
Ala Ser Gly Gly Leu Val Gly Val Tyr Asn Gly Lys Ser Leu Val Phe
115 120 125
      115
                         120
                                          125
Glu Glu Ser Ser Trp Phe Val Ile Asn Val Ile Lys Leu Val Trp Arg
  130.
                    135
                                     140
Tyr Gly Phe Gln Ser Leu Arg Met His Met Trp Val Glu Asp Leu Leu
               150
                                    155
                                                       160
Asp Lys Phe Met Arg Ile Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe
              165
                                170
                                                  175
Ser Ser Val Glu Lys Leu Met His Ala Ile Gly Gly Asp Asp Tyr Val
```

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180
                             185
                                                190
Arg Leu Leu Asn Gln Thr Leu Arg Glu Asn Leu Lys Lys Ala Gly Phe
    195
                       200
                                           205
Ser Glu Thr Phe Leu Asn Glu Met Ile Ala Pro Val Met Lys Val Asn
                    215
                                   220
Tyr Gly Gln Ser Thr Asp Ile Asn Ala Phe Val Gly Ala Val Ser Leu
225
       230
                                    235
Thr Ala Ala Asp Ser Asn Leu Trp Ala Val Glu Gly Gly Asn Lys
              245
                                 250
<210> 707
<211> 150
<212> PRT
<213> Mouse
<400> 707
Met Ser Trp Trp Arg Asp Asn Phe Trp Ile Ile Leu Ala Met Ser Ile
Ile Phe Ile Ser Leu Val Leu Gly Leu Ile Leu Tyr Cys Val Cys Arg
      20
                             25
Trp Gln Leu Arg Gln Gly Arg Asn Trp Glu Ile Ala Lys Pro Ser Lys
   35
                         40
                                            45
Gln Asp Gly Arg Asp Glu Glu Lys Met Tyr Glu Asn Val Leu Asn Ser
  50
                     55
                                        60
Ser Pro Gly Gln Leu Pro Ala Leu Pro Pro Arg Gly Ser Pro Phe Pro
              70
                                   75
Gly Asp Leu Ala Pro Gln Glu Ala Pro Arg Gln Pro Ser Ala Trp Tyr
             85
                               90
                                                95
Ser Ser Val Lys Lys Val Arg Asn Lys Lys Val Phe Ala Ile Ser Gly
         100
                          105
                                     110
Ser Thr Glu Pro Glu Asn Asp Tyr Asp Asp Val Glu Ile Pro Ala Thr
  115
                        120
                                      125
Thr Glu Thr Gln His Ser Lys Thr Thr Pro Phe Trp Gln Ala Glu Val
130 135 140
Gly Leu His Ser Ser Phe
145
                  150
<210> 708
<211> 114
<212> PRT
<213> Mouse
<400> 708
Met Phe Leu Val Tyr Phe Ser Arg Arg Gly His Cys Ile Asn Tyr Val
              5
                                10
Lys Gly His Ala Asp Ser Leu Ala Pro Trp Cys Cys Gly Val Gly Leu
      20
                             25
Arg Ser Pro Leu Ala Arg Pro Gln His Gly His Val Ser Pro Lys Asp
     35
                      40
His Val Pro Gly Gly His Ala Pro Gly Pro Ser His Lys Trp Leu Cys
                  55
Thr Ala Ala Leu Trp Arg Tyr Leu Glu His Ser Ala Val Thr His Gly
                  70
                                   75
Thr Ala Leu Pro Glu Ala His Ala Val Arg Gly Lys His Gly Lys Lys
                               90
                                                  95
Gly Arg Arg Val Val Cys Cys Ser Val Asp Phe Pro Gln Ala Thr Ser
          100
                             105
```

Leu Phe

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<210> 709
<211> 132
<212> PRT
<213> Mouse
<400> 709
Ala His Pro Arg Pro Gly Ala Arg Arg Pro Arg Leu Leu Ala Phe Gln
                                  10
Ala Ser Cys Ala Pro Ala Pro Gly Ser Arg Asp Arg Cys Pro Glu Glu
          20
                              25.
Gly Gly Pro Arg Cys Leu Arg Val Tyr Ala Gly Leu Ile Gly Thr Val
      35
                          40
Val Thr Pro Asn Tyr Leu Asp Asn Val Ser Ala Arg Val Ala Pro Trp
  50
                   . 55
                                         60
Cys Gly Cys Ala Ala Ser Gly Asn Arg Arg Glu Glu Cys Glu Ala Phe
                 70
                                      75
Arg Lys Leu Phe Thr Arg Asn Pro Cys Leu Asp Gly Ala Ile Gln Ala 85 90 95
              85
                                 90
Phe Asp Ser Leu Gln Pro Ser Val Leu Gln Asp Gln Thr Ala Gly Cys
                            105
                                              110
Cys Phe Pro Arg Val Ser Trp Leu Tyr Ala Leu Thr Ala Leu Ala Leu
      115
                           120
Gln Ala Leu Leu
   130
<210> 710
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<212> PRT
<213> Mouse
<400> 710
Met Arg Val Leu Trp Val Leu Gly Leu Cys Cys Val Leu Leu Thr Phe
                                  10
                                                     15
Gly Phe Val Arg Ala Asp Asp Glu Val Asp Val Asp Gly Thr Val Glu
     20
                              25
Glu Asp Leu Gly Lys Ser Arg Glu Gly Ser Arg Thr Asp Asp Glu Val
     35
                          40
Val Gln Arg Glu Glu Glu Ala Ile Gln Leu Asp Gly Leu Asn Ala Ser
   50
                     55
                                         60
Gln Ile Arg Glu Leu Arg Glu Lys Ser Glu Lys Phe Ala Phe Gln Ala
                  70
                                    75
Glu Val Asn Arg Met Met Lys Leu Ile Ile Asn Ser Leu Tyr Lys Asn
              85
                                  90
                                                     95
Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser Asp Ala Leu
          100
                             105
                                                 110
Asp Lys Ile Arg Leu Ile Ser Leu Thr Asp Glu Asn Ala Leu Ala Gly
       115
                         120
                                             125
Asn Glu Glu Leu Thr Val Lys Ile Lys Cys Asp Lys Glu Lys Asn Leu
  130
                      135
Leu His Val Thr Asp Thr Gly Val Gly Met Thr Arg Glu Glu Leu Val
                  150
                                   155
Lys Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Ser Glu Phe Leu Asn
               165
                                 170
                                                    175
Lys Met Thr Glu Ala Gln Glu Asp Gly Gln Ser Thr Ser Glu Leu Ile
```

```
180
                             185
                                               190
Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Phe Leu Val Ala Asp Lys
    195
                      200
Val Ile Val Thr Ser Lys His Asn Asn Asp Thr Gln His Ile Trp Glu
                    215
                                       220
Ser Asp Ser Asn Glu Phe Ser Val Ile Ala Asp Pro Arg Gly Asn Thr
225 230
                                   235
Leu Gly Arg Gly Thr Thr Ile Thr Leu Val Leu Lys Glu Glu Ala
              245
                               250
<210> 711
<211> 224
<212> PRT
<213> Mouse
<400> 711
Met Ala Leu Leu Ile Ser Leu Pro Gly Gly Thr Pro Ala Met Ala Gln
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Val Leu Leu Leu Ser Ser Gly Cys Leu His Ala Gly Asn Ser Glu
                            25
                                               30
Arg Tyr Asn Arg Lys Asn Gly Phe Gly Val Asn Gln Pro Glu Arg Cys
      35
                         40
                                           45
Ser Gly Val Gln Gly Gly Ser Ile Asp Ile Pro Phe Ser Phe Tyr Phe
                   55
                                     60
Pro Trp Lys Leu Ala Lys Asp Pro Gln Met Ser Ile Ala Trp Lys Trp
                  70
                                    75
Lys Asp Phe His Gly Glu Val Ile Tyr Asn Ser Ser Leu Pro Phe Ile
             85
                               90
His Glu His Phe Lys Gly Arg Leu Ile Leu Asn Trp Thr Gln Gly Gln
          100
                           105
Thr Ser Gly Val Leu Arg Ile Leu Asn Leu Lys Glu Ser Asp Gln Ala
      115
                     120
                                          125
Gln Tyr Phe Ser Arg Val Asn Leu Gln Ser Thr Glu Gly Met Lys Leu
 130
            · 135
                                140 ·
Trp Gln Ser Ile Pro Gly Thr Gln Leu Asn Val Thr Gln Ala Leu Asn
145
        150
                                   155
Thr Thr Met Arg Ser Pro Phe Ile Val Thr Ser Glu Phe Thr Thr Ala
            165 170 175
Gly Leu Glu His Thr Ser Asp Gln Arg Asn Pro Ser Leu Met Asn Leu
          180
                           185
                                              190
Gly Ala Met Val Thr Met Leu Leu Ala Lys Val Leu Val Ile Val Leu
    195
                        200 .
Val Tyr Gly Trp Met Ile Phe Leu Arg Trp Lys Gln Arg Pro Ala His
   210 ·
                     215
                                        220
<210> 712
<211> 133
<212> PRT
<213> Mouse
<400> 712
Met Ala Leu Pro Trp Thr Ile Leu Leu Ala Leu Ser Gly Ile Tyr Val
               5
                               10
Gln Gly Ala Gln Ala Trp Cys Ser Glu Glu Asp Thr Leu Glu Leu Asp
          20
                           25
                                              30
Lys Leu Val Ser Glu Pro Asp Ile Val Lys Phe Ala Leu Ser Ala Phe
                         40
```

```
His Lys Lys Ser Lys Asp Glu Tyr Ala Tyr Arg Val Ile His Ile Met
   50
                   55
                                     60
Asn Phe Leu Lys Val Gln Glu Glu Pro Pro Gln Thr Phe Phe Val Lys
              70
                                 75
Leu Arg Leu Thr Arg Thr Ile Cys Met Lys Phe Glu Lys Ser Leu Asp
            85
                             90
Thr Cys Pro Leu Pro Glu Leu Gln Asn Ile Leu Ile Cys Ser Phe Ser
     100 105
                                           110
Ile Ser Ser Pro Gly Ser Lys Gln Phe Asn Leu Leu Lys Met Thr Cys
  115
                      120
Ser Glu Gly Leu Leu
  130
<210> 713
<211> 255
<212> PRT
<213> Mouse
<400> 713
Glu Glu Glu Asp Leu Arg Arg Leu Lys Tyr Phe Phe Met Ser Pro
                    10
1 . 5
Cys Asp Lys Phe Arg Ala Lys Gly Arg Lys Pro Cys Lys Leu Met Leu
         20
                          25
                                           30
Gln Val Val Lys Ile Leu Val Val Thr Val Gln Leu Ile Leu Phe Gly
  35 -
                       40
                                        45
Leu Ser Asn Gln Leu Val Val Thr Phe Arg Glu Glu Asn Thr Ile Ala
            55
 50
                                  60
Phe Arg His Leu Phe Leu Leu Gly Tyr Ser Asp Gly Ser Asp Asp Thr
65 70
                                 75
                                               80
Phe Ala Ala Tyr Thr Gln Glu Gln Leu Tyr Gln Ala Ile Phe Tyr Ala
           85
                             90
Val Asp Gln Tyr Leu Ile Leu Pro Glu Ile Ser Leu Gly Arg Tyr Ala
       100
                   105
                                           110
Tyr Val Arg Gly Gly Gly Pro Trp Ala Asn Gly Ser Ala Leu Ala
115 120 125
Leu Cys Gln Arg Tyr Tyr His Arg Gly His Val Asp Pro Ala Asn Asp
  130 135
                               140
Thr Phe Asp Ile Asp Pro Arg Val Val Thr Asp Cys Ile Gln Val Asp
                150
                               155
Pro Pro Asp Arg Pro Pro Asp Ile Pro Ser Glu Asp Leu Asp Phe Leu
            165
                     170
                                              175
Asp Gly Ser Ala Ser Tyr Lys Asn Leu Thr Leu Lys Phe His Lys Leu
       180
                          185
                                   · 190
Ile Asn Val Thr Ile His Phe Gln Leu Lys Thr Ile Asn Leu Gln Ser
   195
                      200
                                       205
Leu Ile Asn Asn Glu Ile Pro Asp Cys Tyr Thr Phe Ser Ile Leu Ile
 210
                   215
                                   220
Thr Phe Asp Asn Lys Ala His Ser Gly Arg Ile Pro Ile Arg Leu Glu
225
               230 235
Thr Lys Thr His Ile Gln Glu Cys Lys His Pro Ser Val Ser Arg
             245
                              250
                                               255
<210> 714
<211> 255
<212> PRT
<213> Mouse
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Met Asn Ile Val Val Glu Phe Phe Val Val Thr Phe Lys Val Leu Trp
                                10
Ala Phe Val Leu Ala Ala Ala Arg Trp Leu Val Arg Pro Lys Glu Lys
                            25
Ser Val Ala Gly Gln Val Cys Leu Ile Thr Gly Ala Gly Ser Gly Leu
  . 35
                       40
                                         45
Gly Arg Leu Phe Ala Leu Glu Phe Ala Arg Arg Arg Ala Leu Leu Val
   50
                55
Leu Trp Asp Ile Asn Thr Gln Ser Asn Glu Glu Thr Ala Gly Met Val
            70
                                   75
Arg His Ile Tyr Arg Asp Leu Glu Ala Ala Asp Ala Ala Ala Leu Gln
             85
                               90
Ala Gly Lys Gly Glu Glu Glu Ile Leu Pro Pro Cys Asn Leu Gln Val
         100
                            105
                                     110
Phe Thr Tyr Thr Cys Asp Val Gly Lys Arg Glu Asn Val Tyr Leu Thr
     115
                       120
                                   125
Ala Glu Arg Val Arg Lys Glu Val Gly Glu Val Ser Val Leu Val Asn
             135
                                     140
Asn Ala Gly Val Gly Ser Gly His His Leu Leu Glu Cys Pro Asp Glu
145 150 155 160
Leu Ile Glu Arg Thr Met Met Val Asn Cys His Ala His Phe Trp Thr
             165
                              170
                                        175
Thr Lys Ala Phe Leu Pro Thr Met Leu Glu Ile Asn His Gly His Ile
          180
                            185
                                             190
Val Thr Val Ala Ser Ser Leu Gly Leu Phe Ser Thr Ala Gly Val Glu
      195
                        200
                                          205
Asp Tyr Cys Ala Ser Lys Phe Gly Val Val Gly Phe His Glu Ser Leu
  210
                    215
                                       220
Ser His Glu Leu Lys Ala Ala Glu Lys Asp Gly Ile Lys Thr Thr Leu
                230
                                   235
Val Cys Pro Tyr Leu Val Asp Thr Gly Met Phe Arg Gly Cys Arg
 . 245
                                250
<210> 715
<211> 200
<212> PRT
<213> Mouse
<400> 715
Met Phe Pro Lys Asn Ser Arg Cys Pro Thr Cys Asp Leu Arg Lys Pro
          5
                        10
Ala Arg Ser Lys His Cys Arg Leu Cys Asp Arg Cys Val His Arg Phe
                          25
Asp His His Cys Val Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Thr
    35
                        40
                                          45
Arg Tyr Phe Leu Ile Tyr Leu Leu Thr Leu Thr Ala Ser_Ala Ala Thr
  50
                   55
Ile Ala Thr Val Thr Ala Ala Phe Leu Leu Arg Leu Val Thr Val Ser
               70
                                  75
Asp Leu Tyr Gln Glu Thr Tyr Leu Asp Asp Val Gly His Phe Gln Ala
             85
                               90
Val Asp Thr Val Phe Leu Ile Gln His Leu Phe Leu Ala Phe Pro Arg
        100 ·
                          105
Ile Val Phe Leu Leu Gly Phe Val Ile Val Leu Ser Met Leu Leu Ala
       115
                       120
                                        125
```

Gly Tyr Leu Cys Phe Ala Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr

```
130
                      135
                                        140
Asn Glu Trp Tyr Lys Gly Asp Trp Ala Trp Cys Gln Arg Trp Pro Leu
145
                150
                              155
                                                    1.60
Val Ala Trp Ser Pro Ser Ala Glu Pro Arg Ile His Gln Asn Ile His
             165
                              170
                                                175
Ser His Gly Phe Arg Ser Asn Leu Arg Glu Ile Phe Leu Pro Ala Thr
                   185
          180
Pro Ser Tyr Lys Lys Lys Glu'Lys
       195
<210> 716
<211> 115
<212> PRT
<213> Mouse
<400> 716
Gly Glu Leu Arg Ala Leu Leu Ala Phe Thr His Leu Ser Ser Ala His
               5
                                 10
Phe Trp Leu Met Met Thr Leu Gly Gly Leu Phe Gly Phe Ala Ile Gly
       20
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                                              30
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245

International application No. PCT/NZ01/00099

			C1/NZ01/00099		
A.	CLASSIFICATION OF SUBJECT MATTER				
Int. Cl. 7:	C12N 15/12, 15/18, 15/19				
According to	International Patent Classification (IPC) or to both	national classification and IPC			
В.					
	umentation searched (classification system followed by c	classification symbols)			
AS BELOW					
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched					
AS BELOW	 base consulted during the international search (name of 	Edata kasa and Juhara masticable s	north terms used)		
	ss Prot, EMBL, Genebank, : SEQ ID. NOS. 1		each terms used)		
C.	DOCUMENTS CONSIDERED TO BE RELEVANT	r			
Category*	Citation of document, with indication, where app	propriate, of the relevant passage	s Relevant to claim No.		
P, X	EP 1 067 182 HELIX RESEARCH INSTIT Sequence Id. 487, & GeneBank Accession I		1 - 3. (SEQ ID NO 1)		
P, X	EP 1067 182 HELIX RESEARCH INSTITUTE Sequence Id. 219, & GeneBank Accession I		1 - 3. (SEQ ID NO 1)		
х	EMBL Accession Number AC008119 (9 Oc 12q24.1-116.6-118.9 BAC RPCI11-951I11	ctober 1999) Homo sapiens	1 - 3. (SEQ ID NO 1)		
X Further documents are listed in the continuation of Box C X See patent family annex					
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art document member of the same patent family					
	Date of the actual completion of the international search Date of mailing of the international search report				
	ling address of the ISA/AU	Authorized officer			
E-man address. percorpaustrana.gov.ad		ALISTAIR BESTOW Telephone No: (02) 6283 2450	; . O		

International application No.

PCT/NZ01/00099

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	US, A, 5 952 486 L. N. BLOKSBERG ET. AL. (14 September 1999) See SEQ ID 53. & GeneBank Accession number AR074144.	1 - 3. (SEQ ID NO 2)		
х	WO, A, 2000 40752 THE NOTTINGHAM TRENT UNIVERSITY (13 July 2000) See SEQ ID NO. 2. & GeneBank Accession Number AX026540.	1 - 3. (SEQ ID NO 2)		
х	EMBL Accession Number UCAJ4935 (2 March 1999.) Urechis caupo mRNA for cytoplasmic intermediate filament protein.	1 - 3. (SEQ ID NO 2)		
х	WO, A, 99 53040 METAGEN GESELLSCHAFT FÜR GENOMFORSCHUNG MBH (21 October 1999) See SEQ ID 31. & GenBank Accession Number AX014842.	1 - 3. (SEQ ID NO 4)		
P, X	WO, A, 2001 07612 INCYTE GENOMICS, INC. (1 February 2001) See SEQ ID 43 & Genebank Accession Number AX078375.	1 - 3. (SEQ ID NO 4)		
P, X	WO, A, 2001 10902 CURAGEN CORPORATION (15 February 2001) See SEQ ID 5 & Genebank Accession Number AX084211.	1 - 3. (SEQ ID NO 5)		
Х	EMBL Accession Number AF169677 (29 JANUARY 2000) Homo sapiens leucine-rich repeat transmembrane protein FLRT3 (FLRT3) mRNA, complete cds.	1 - 3. (SEQ ID NO 5)		
Х	EMBL Accession Number RNMOG (20 August 1992) Rattus norvegicus myelin/oligodendrocyte glycoprotein (MOG) gene, complete cds.	1 - 3. (SEQ ID NO 7)		
A	EMBL Accession Number D50030 (14 April 2000) Homo sapiens gene for hepatocyte growth factor activator, complete cds.	1 - 3. (SEQ ID NO 8)		
Х	WO, A, 99 55865 GENESIS RESEARCH AND DEVELOPMENT CORPORATION LIMITED (4 November 1999) See SEQ ID NOS 1 - 10, 147, 187, 196, 294, 295 and 395.	1 - 3, 8-17, 27-29 (SEQ ID NOS 1-10, 147, 196, 294, 295, 413-5, 417)		
P, X	WO, A, 2000 69884 GENESIS RESEARCH AND DEVELOPMENT CORPORATION LIMITED (23 November 2000) See SEQ ID NOS 1 - 10, 147, 187, 196, 294, 295 and 395.	1 - 3, 8-17, 27-29 (SEQ ID NOS 1-10, 147, 196, 294, 295, 413-5, 417)		

International application No. PCT/NZ01/00099

PC1/42/01/00099				
C (Continua	tion) DOCUMENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
PX	WO, A, 00 63230 HUMAN GENOME SCIENCES, INC. (26 October 2000) See SEQ ID NO 68 and pages 16-29	1-3, 8-17, 27- 29 (SEQ ID NOS 196, 413-5, 417		
х	WO, A, 00 29438 MILLENNIUM PHARMACEUTICALS, INC. (25 May 2000) See Figures 1, 3, 5,7 and 8	1-3, 8-17, 27- 29 (SEQ ID NOS 196, 413-5, 417		
PX	WO, A, 00 63377 ZYMOGENETICS, INC. (26 October 2000) See SEQ ID NOS 1 and 11	1-3 (SEQ ID NO 147, 294		
PX	WO, A, 01 49728 PROTOGENE, INC. (12 July 2001) See SEQ ID NO 59 and Table 1	1-3 (SEQ ID NO 147)		
PX	WO, A, 00 73448 ZYMOGENETICS, INC. (7 December 2000) Sec SEQ ID NOS 1 and 14	1-3 (SEQ ID NO 294)		
х	GenPept Accession No. CAB53702 (18 February 2000) Hypothetical Protein Homo sapiens Ottenwaelder B et al	1-3 (SEQ ID NO 295)		
		i		

International application No.

PCT/NZ01/00099

Box I	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This inter	national search report has not been established in respect of certain claims under Article 17(2)(a) for the following
1.	Claims Nos:
	because they relate to subject matter not required to be searched by this Authority, namely:
2.	Claims Nos: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3.	Claims Nos:
	because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)
Вох П	Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This Inter	national Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
	1-3, 8-17 and 27-29 (SEQ ID NOS 1-10, 147, 196, 294, 295, 413-415, 417)
	More than one invention has been claimed. (continued in supplemental box
4.	No required additional search fees were timely paid by the applicant.
Remark o	n Protest
	No protest accompanied the payment of additional search fees.

International application No.

PCT/NZ01/00099

Supplemental B x

(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No: II

Rule 13.1 of the PCT states the principle that an International Application should relate to only one invention or, if there is more than one invention, that the inclusion of those inventions in one International Application is only permitted if all inventions are so linked to form a single general inventive concept. Rule 13.2 of the PCT defines the method for determining whether the requirement of unity of invention is satisfied in respect of a group of inventions claimed in the International application. Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding "special technical features." The expression "special technical features" is defined in Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made on the contents of the claims as interpreted in the light of the description and drawings (if any).

There is no special technical feature which is common to all 725 sequences disclosed in the specification. It is well known in the art that for a given cell type, the cell will express a great many sequences, each having a different function from the others. That they are sourced from skin, cells is not a special technical feature. For applications claiming nucleotides and peptides, there are two features which are to be considered for the purposes of determining the number of inventions in a specification.

1) If the polynucleotide has a corresponding peptide, then the two sequences may have a common special technical feature because the nucleotide encodes the peptide. Therefore they are regarded as a single invention.

In the present case, the specification does not disclose a complete concordance between the polynucleotides and corresponding polypeptides, other than those disclosed in Table 2. While Table 2 purports to provide a concordance between nucleotides and peptides for which they code, this is incomplete, as the majority of sequences are not referred to on this table. Therefore the ISA is unable to confidently determine the number of inventions, on the basis of a concordance between the polynucleotides and the peptides.

2) A group of two or more nucleotides, or two or more peptides, which share a significant structural element. A "significant structural element" is the structural element that defines the specific biological activity of an amino acid sequence or a nucleotide sequence or its encoded polypeptide and is disclosed as the feature that defines the contribution which each of the inventions, considered as a whole, makes over the prior art. If each of the inventions shares the same significant structural element, then it provides the special technical feature which is required to establish unity of invention.

In the present case, genes and their expressed proteins from skin cells have been sequenced. The applicant has provided no evidence that the nucleotide sequences of the present application, and the peptides they express, all form a group of protein types sharing a significant structural element. On the contrary, the putative peptides derived from the nucleotide sequences of the application have a wide range of functions based on their similarity to known proteins. (see Table 2) At best, it appears from Table 2 that there may be 76 distinct protein types which share a common function, and therefore may share a common significant structural element. However, most of the polynucleotides and peptides which do not appear on Table 2, have not have been identified in terms of their function, much less, whether any of them have a shared significant structural element. Therefore, the ISA is unable to confidently determine the number of inventions, on the basis of a shared significant structural element. Thus, at this stage, in the absence of a complete polynucleotide peptide concordance, or the definition of a special technical feature which is common to two or more sequences, this ISA considers that that there are 72 groupings of sequences, which encompass the 725 sequences.

While the ISA is unable to determine the precise number of inventions in this application it is prepared, as a service, to search a first group of ten sequences for a single search fee. This offer is provided purely as a service to the applicant and should not be taken as having any bearing on the ISA's assessment of the number of inventions claimed in these 10 sequences. The ISA also agrees to search the two further inventions specified by the applicant in their letter of 30 August 2001, for two additional search fees. As such, the ISA has searched SEQ ID NOS 1-10, 147, 196, 294, 295, 413-5 and 417.